COVID Vaccine in Pregnancy

Dr. Marjorie Meyer

November 16, 2021

VCHIP
Vermont Child Health Improvement Program
UNIVERSITY OF VERMONT LARNER COLLEGE OF MEDICINE

PERINATAL QUALITY COLLABORATIVE VERMONT

Reminders

- Please mute yourself upon entry and keep yourself muted while listening.
- You are welcome to ask questions throughout the presentation. Feel free to use the chat function, raise your hand, or unmute to ask your question directly.
- This presentation will be recorded and will be available for view. The recording will be emailed out to participants tomorrow along with a short satisfaction survey.

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PERINATAL QUALITY COLLABORATIVE VERMONT

COVID and COVID Vaccine: Prepregnancy, Pregnancy, Lactation

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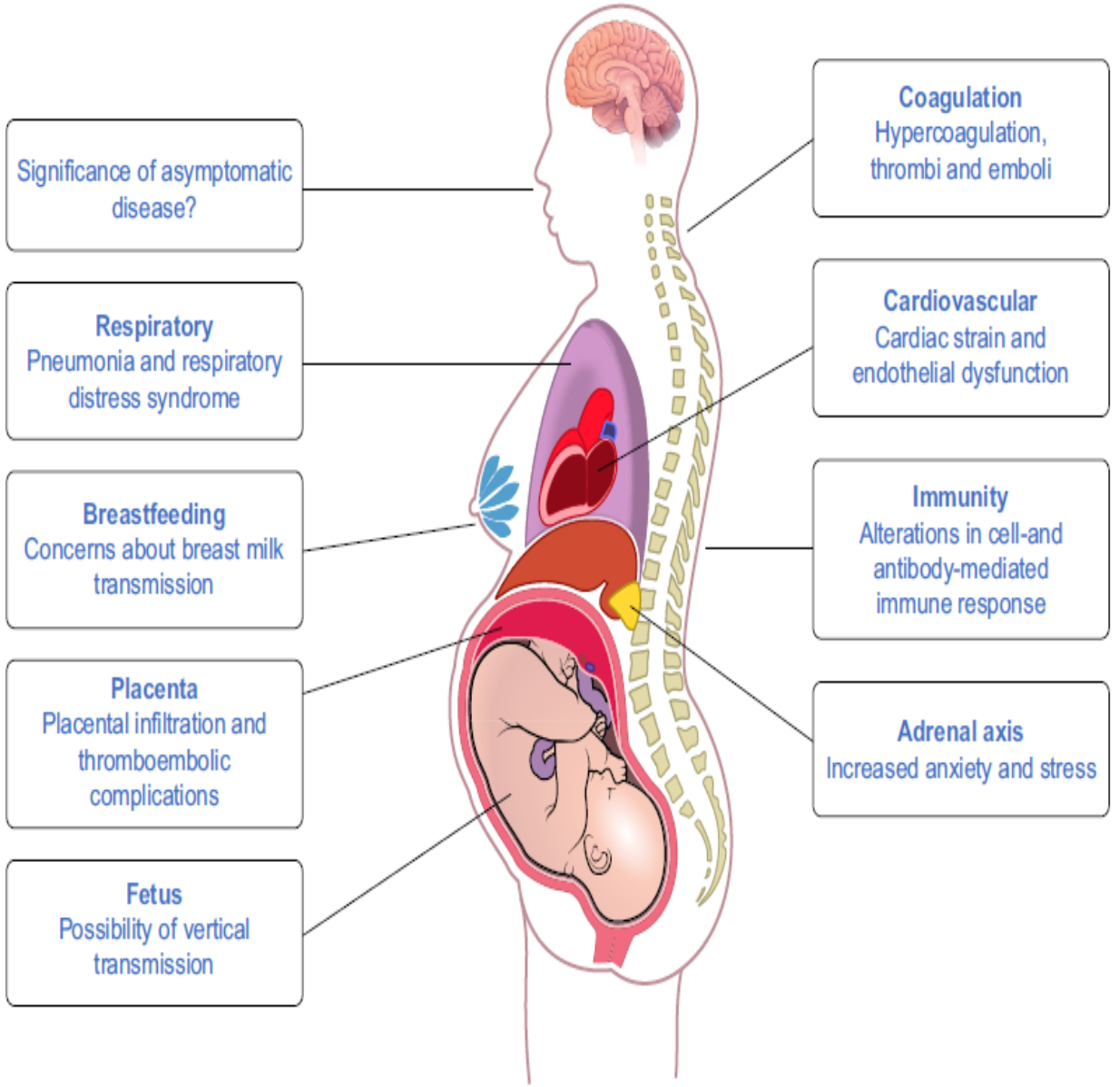

WASTNEDGE ET AL., 2021, *Physiol Rev* 101: 303–318
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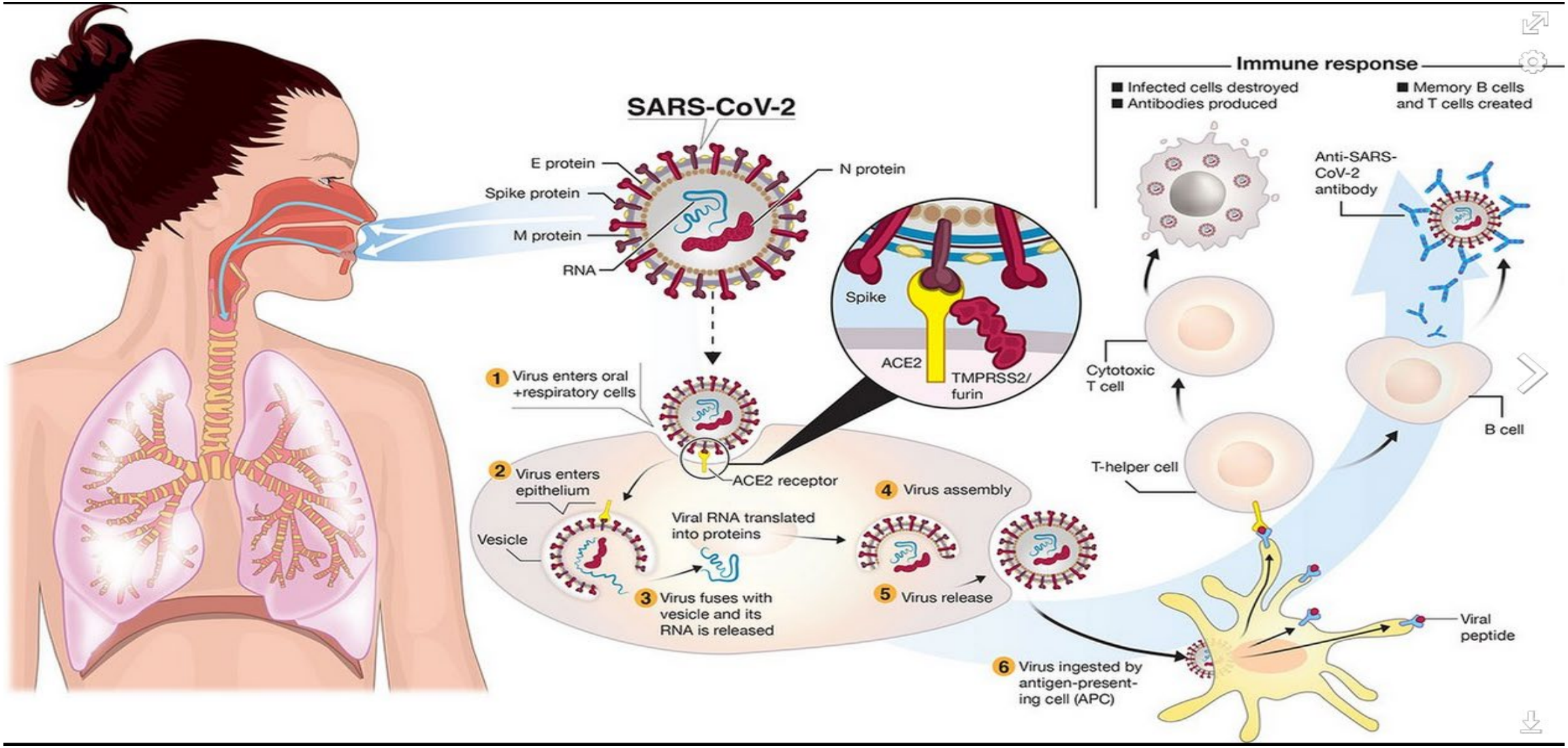
Objectives/Educational Objectives

- Review COVID in pregnancy impact
- Review COVID treatment
- mRNA vaccine physiology
- Review pre-pregnancy vaccine (AKA: general public)
- Review pregnancy vaccine
- Review vaccination during lactation

Disclosures

- none

Pre-pregnancy: COVID infection



https://en.wikipedia.org/wiki/COVID-19#/media/File:Fphar-11-00937-g001.jpg

Progression of COVID-19

I. Early infection

- Virus infiltrates the pulmonary parenchyma and replicates triggering an inflammatory response involving local vasodilation, increased endothelial permeability, leukocyte recruitment

II. Pulmonary involvement

- Shortness of breath, cough, ground glass opacities on lung imaging
- COVID-19 pneumonia
  - May rapidly progress from focal to diffuse bilateral consolidation of lung parenchyma
  - **IIa without hypoxemia** ($PaO_2/FiO_2 \geq 300$ mmHg), $PaO_2 \geq 63$mmHg on RA
  - **IIb with hypoxemia** ($PaO_2/FIO_2 < 300$ mmHg, $PaO_2 < 63$ mmHg on RA)

III. Severe hyperinflammation

- Marked systemic inflammation characterized by a cytokine storm (**IL-6**, IL-2, IL-7, TNF-α, interferon-γ, IP-10, MCP-1, CRP, procalcitonin, **ferritin**)
- Severe damage to lung parenchyma →progressive respiratory distress, multi-organ failure

Pfeifer et al. Respiration. 2020.

Progression of COVID-19

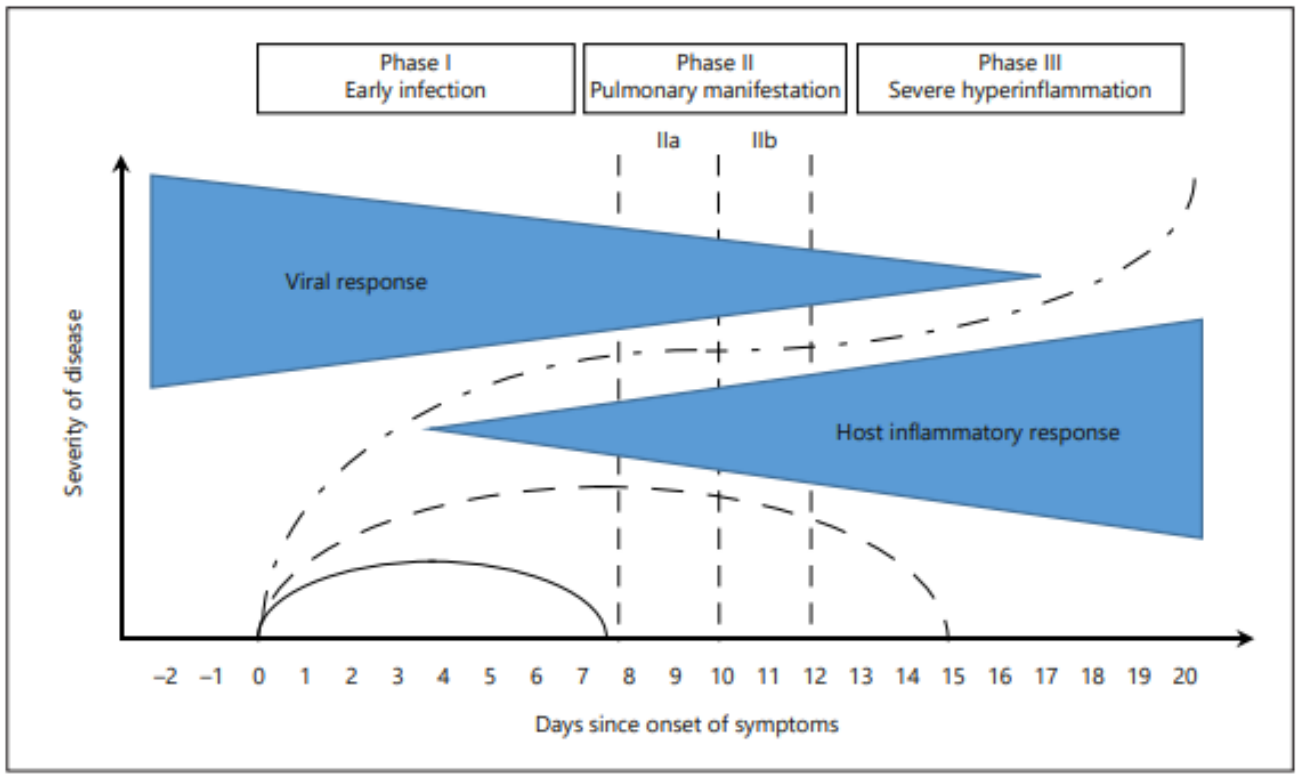
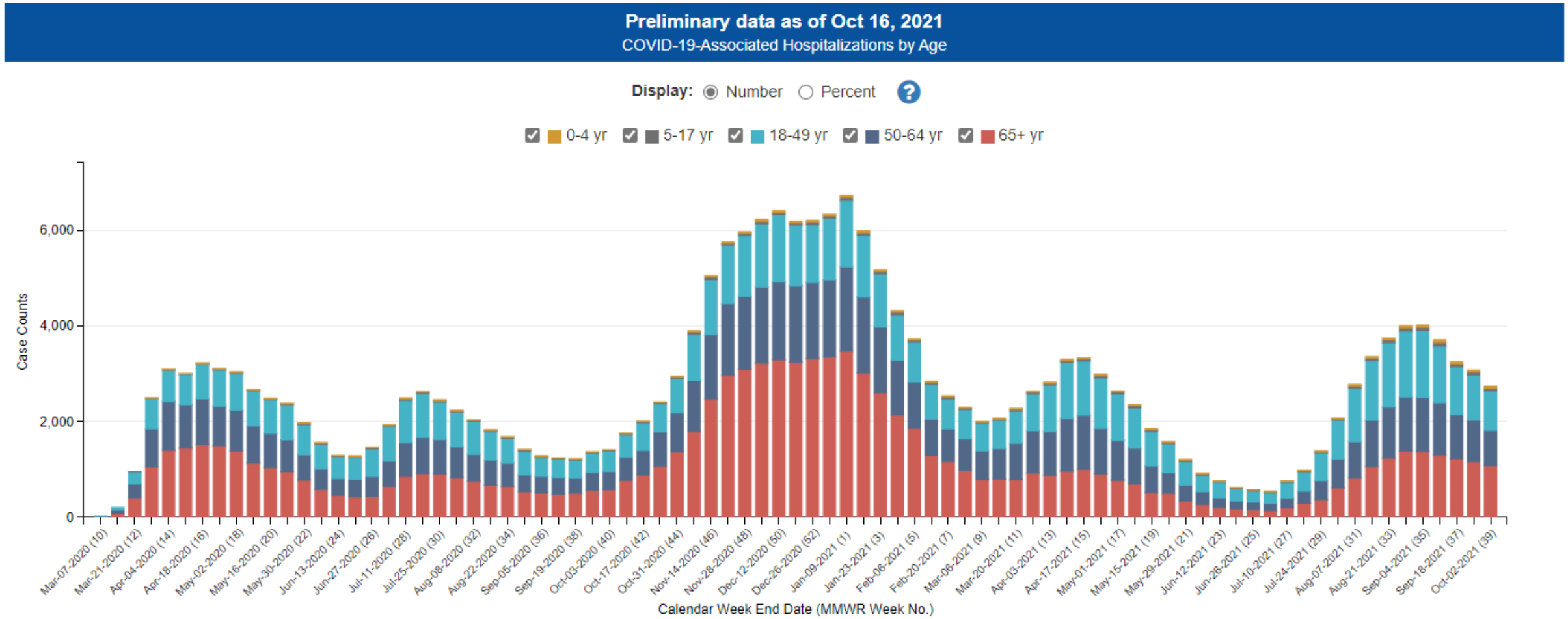


Fig. 1. Significance of immune defense and systemic inflammatory response for the symptoms of COVID-19 patients. Clinical progression of COVID-19 (mild, green; severe, grey; critical, red) over time [14, 15].

Pfeifer et al. Respiration. 2020.

Total COVID cases, all ages: waves are clear

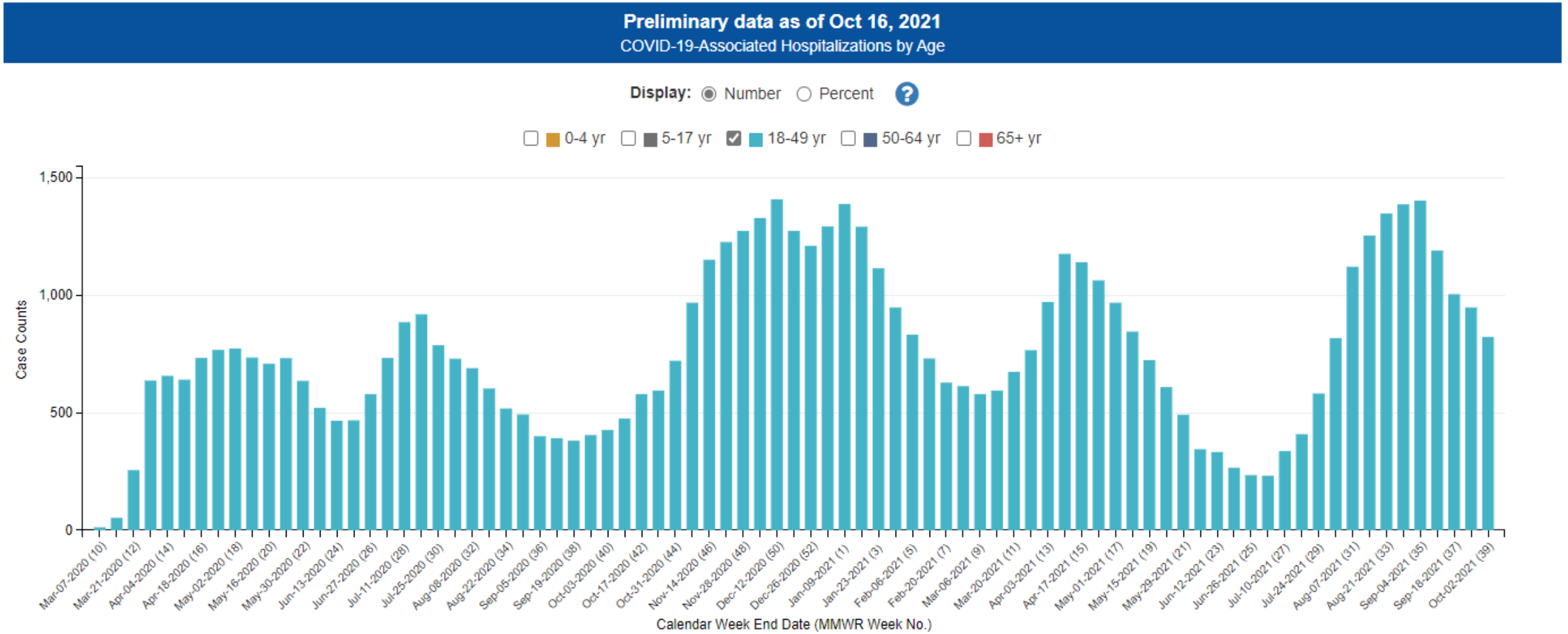


Cumulative case count by age group

	0-4 yr	5-17 yr	18-49 yr	50-64 yr	65+ yr	Total
2020-21	1644	2669	63162	62802	94677	224954

[CDC COVID Data Tracker]

Total COVID cases, reproductive ages: waves are clear

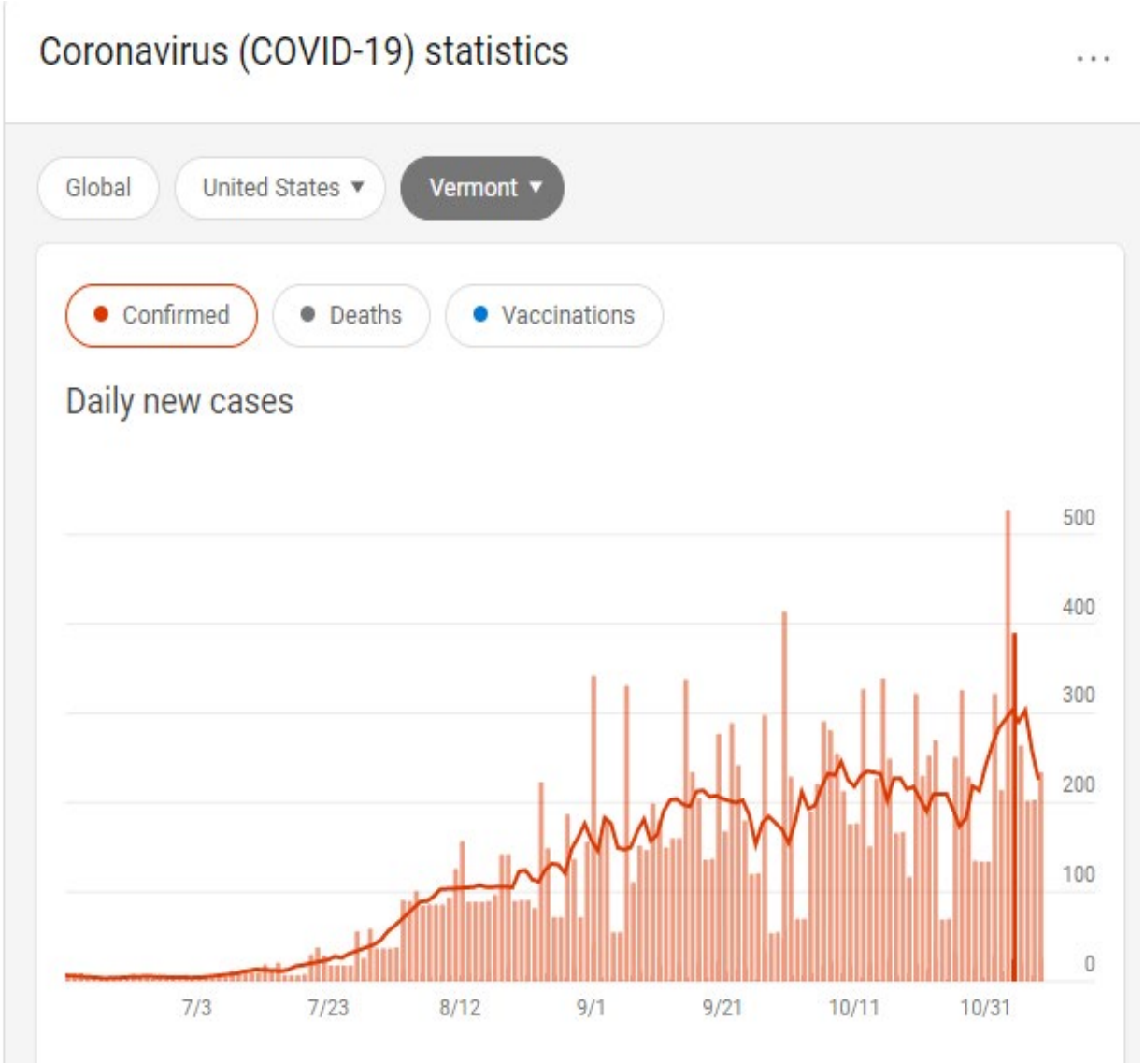


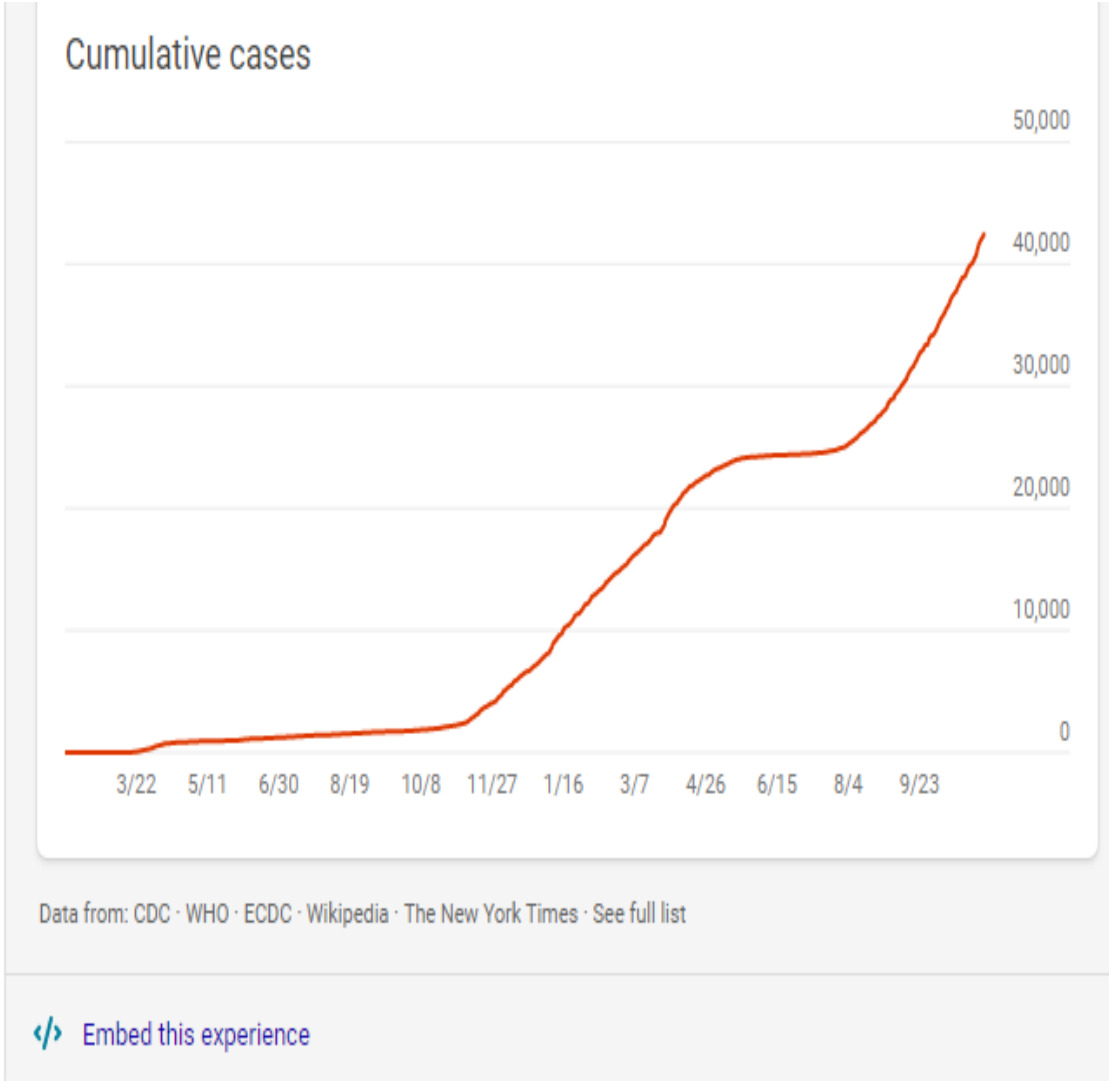
Cumulative case count by age group

	18-49 yr	Total
2020-21	63162	63162

[CDC COVID Data Tracker]

COVID infections are not flattening yet in Vermont

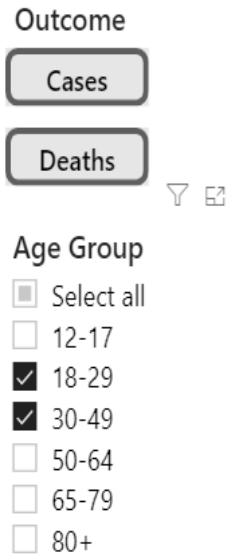


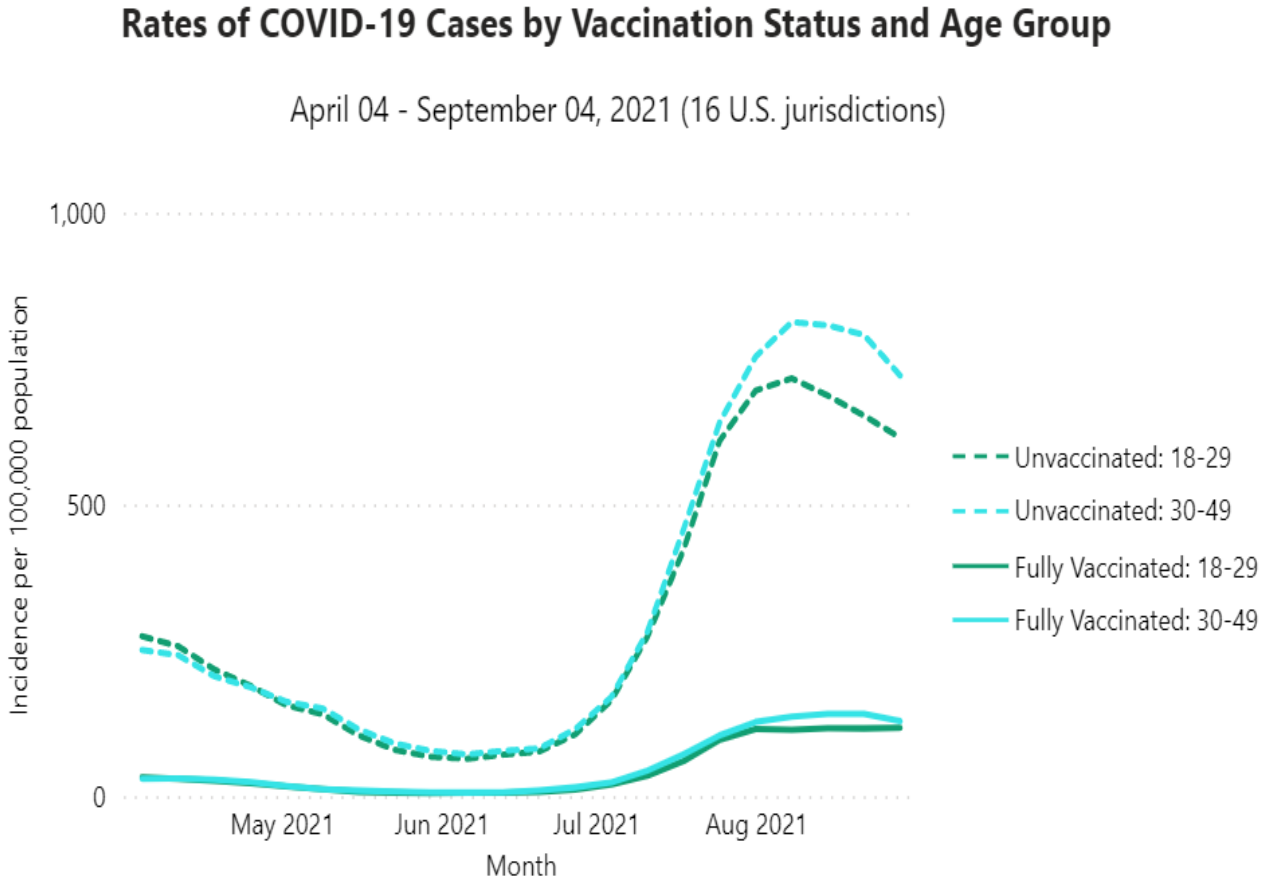


CDC tracker

Vaccination Works:
Reduced risk of testing positive for COVID

- About 750/100,000 people of reproductive age will get COVID (~1%) each month if not vaccinated
- Reproductive aged unvaccinated people are 6x more likely to get infected with COVID





In August, unvaccinated persons had:

6.1X

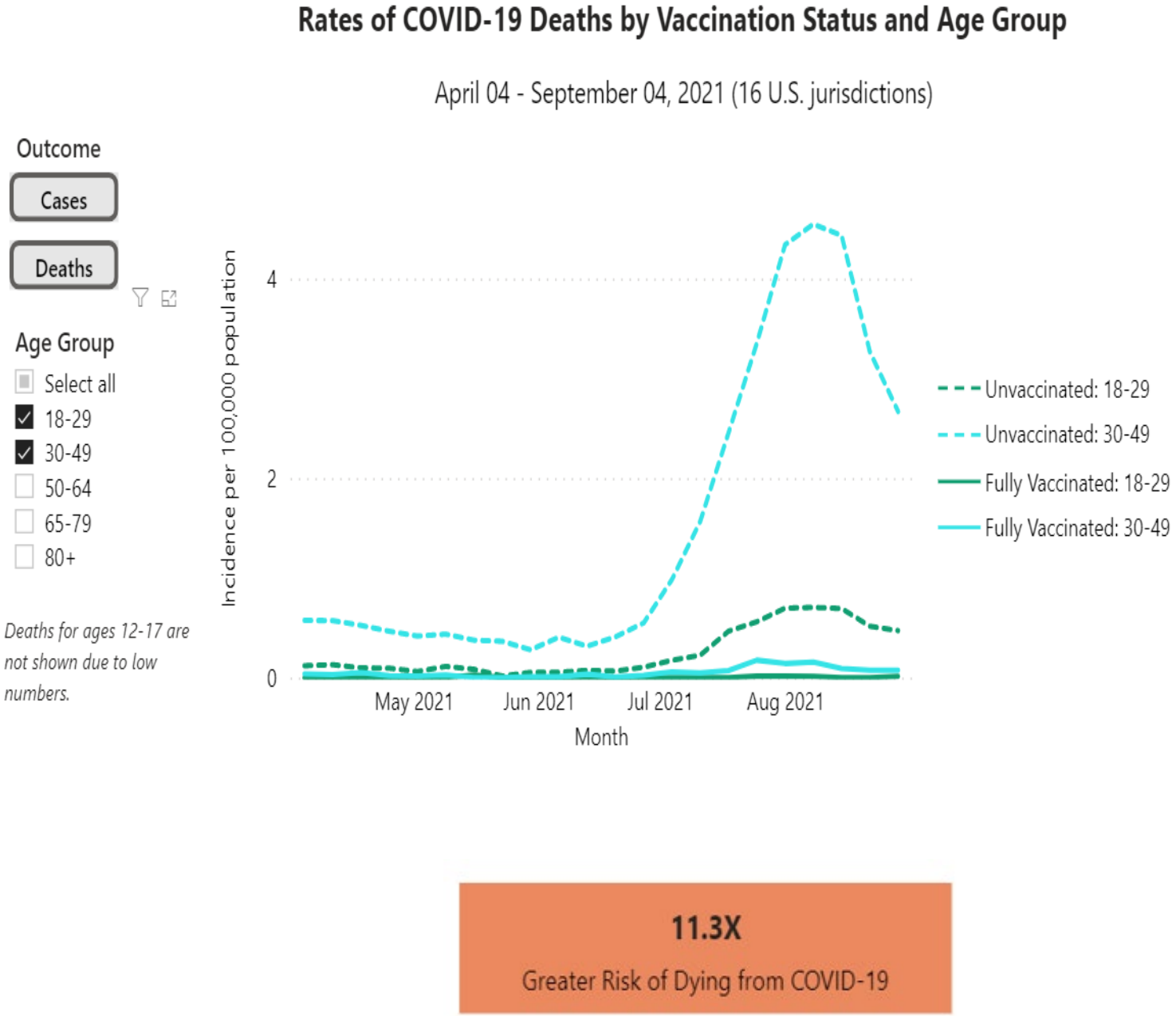
Greater Risk of Testing Positive for COVID-19

compared to fully vaccinated persons

[CDC COVID Data Tracker]

Vaccination Works:
Reduced risk of dying from COVID

- About 4.5/100, 000 people of reproductive age will die each month if not vaccinated
- Reproductive aged unvaccinated people are 11x more likely to die from COVID compared to vaccinated people

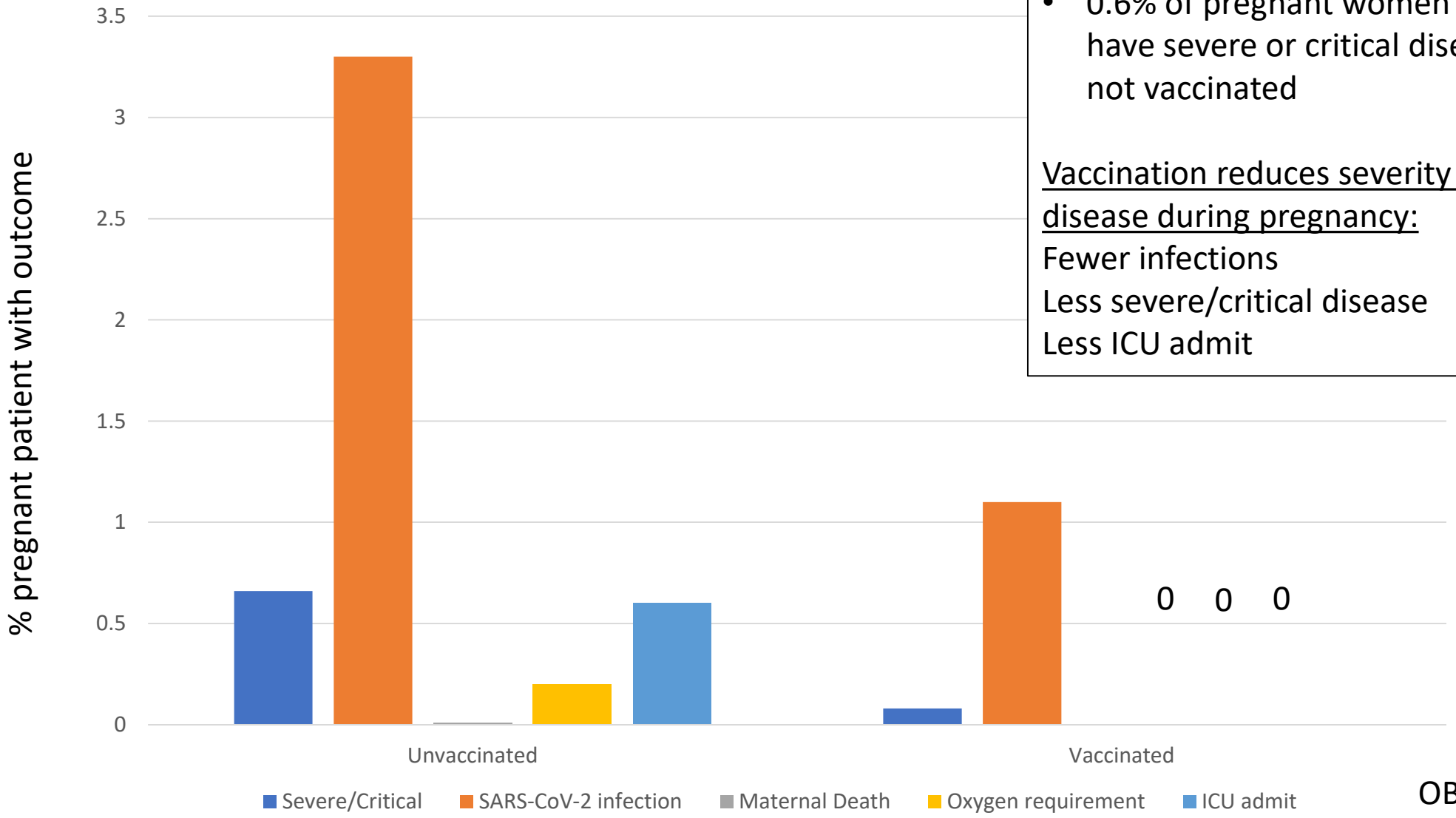


CDC COVID Data Tracker

COVID infection is dangerous for pregnant women

- 3% of pregnant women will get Covid if not vaccinated
- 0.6% of pregnant women will have severe or critical disease if not vaccinated

<u>Vaccination reduces severity of disease during pregnancy:</u>
Fewer infections
Less severe/critical disease
Less ICU admit



OBGYN, epub 10/2021

Pregnant Women with COVID-19 who were hospitalized, UnitedStates, January 22, 2020 - October 18, 2021

Data were collected from 131,512 women, but hospitalization data were only available for 104,230 (79.3%).

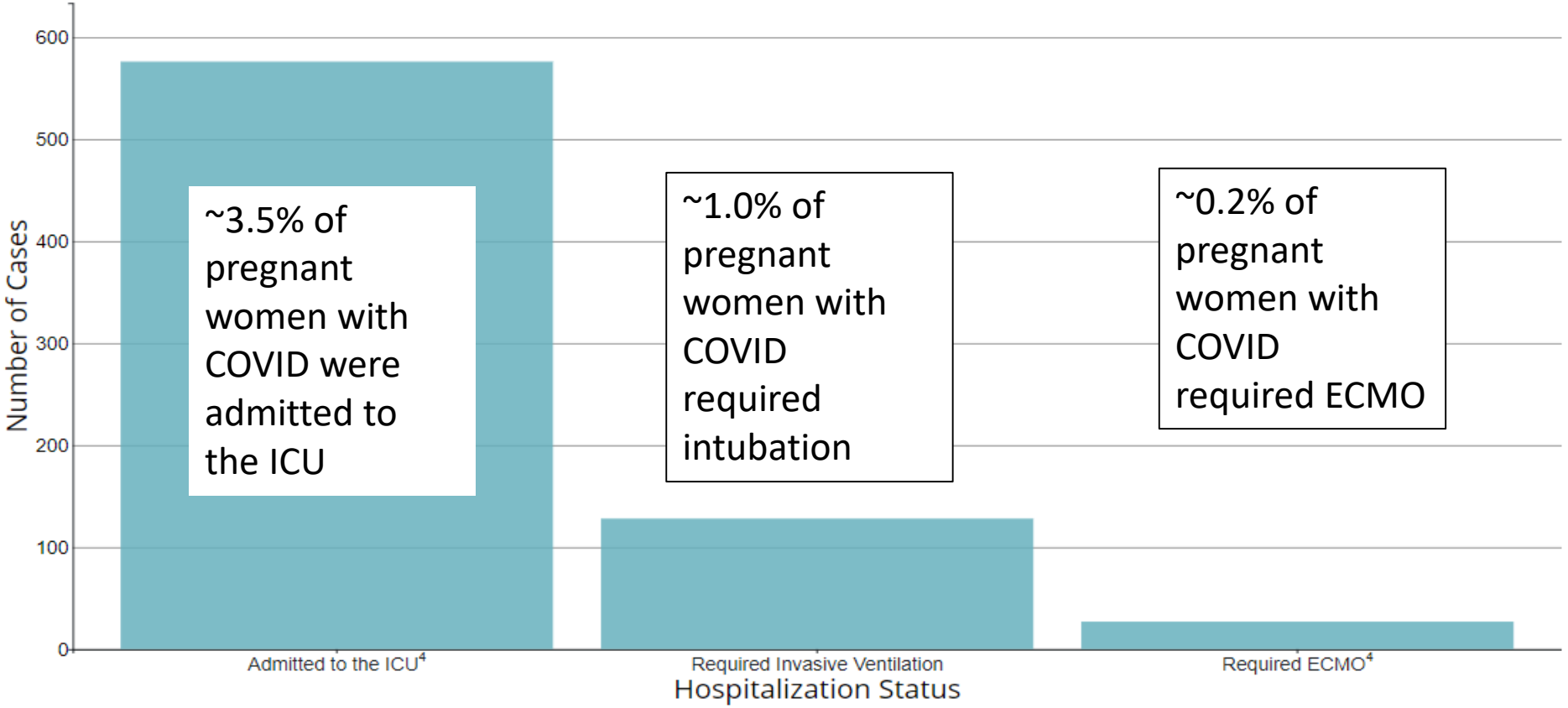
HOSPITALIZED CASES[3]

22,905

22% of pregnant women with COVID were hospitalized

Pregnant women with COVID-19 admitted to the ICU, who required invasive ventilation, or who required ECMO, United States, January 22, 2020 - October 18, 2021

Data were collected from 131,512 women, but ICU admission data were only available for 16,394 (12.5%) women, invasive ventilation data were only available for 11,969 (9.1%) women, and ECMO data were only available for 12,411 (9.4%).

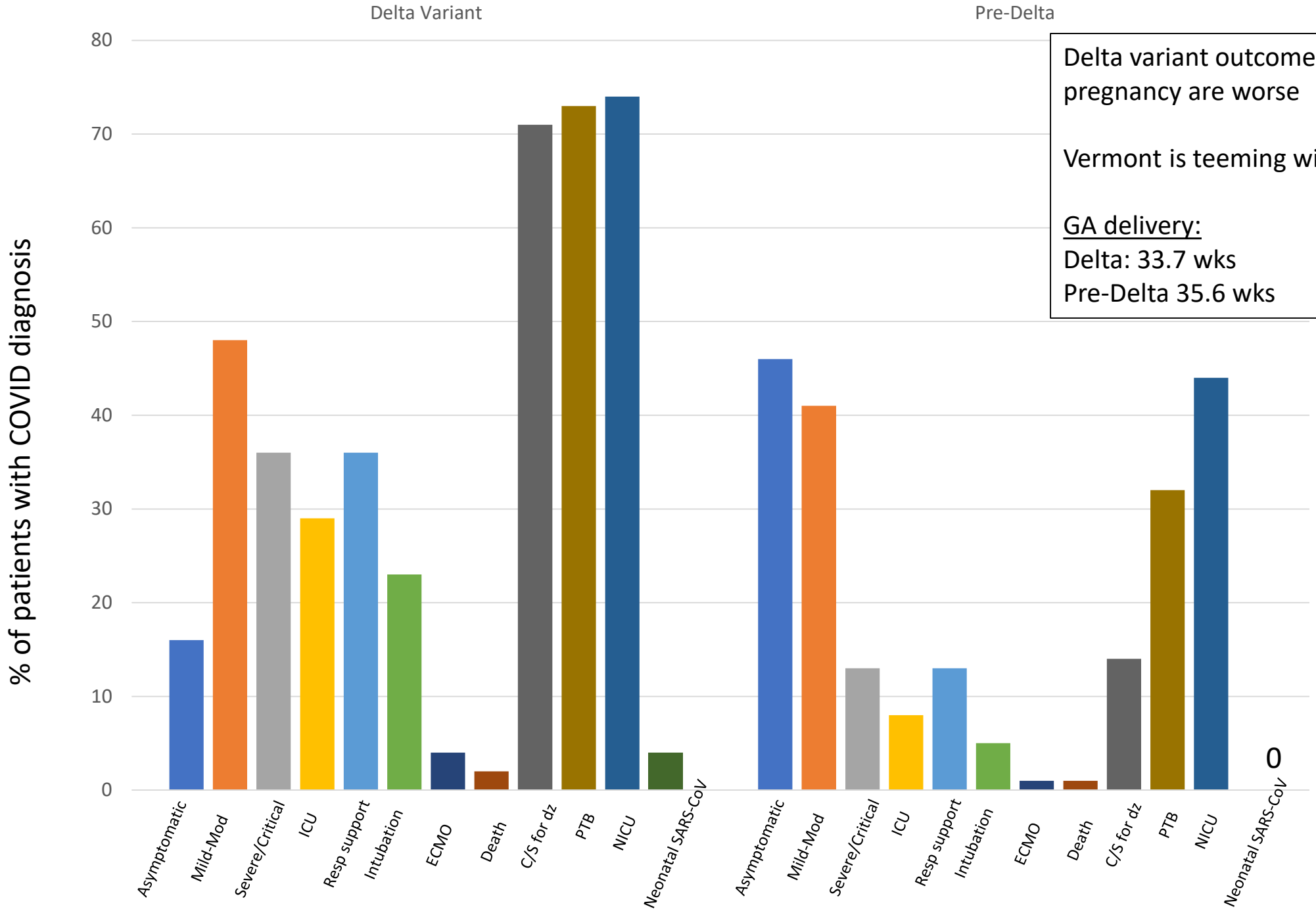


[1]Cases with age <9 years and >54 years are excluded. Cases with unknown age are included.

[2]Other race includes non-Hispanic American Indian or Alaska Native or non-Hispanic Native Hawaiian or Other Pacific Islander

[3] Data were not available to distinguish hospitalization for COVID-19-related indications, such as worsening respiratory status, from hospital admission for pregnancy-related indications, such as delivery.

[4]Abbreviation: ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation, an advanced life support technique used for patients with life-threatening heart and/or lung problems.



Delta variant outcomes during pregnancy are worse

Vermont is teeming with Delta variant

<u>GA delivery:</u>
Delta: 33.7 wks
Pre-Delta 35.6 wks

OBGYN, epub, 2021

What happens when a pregnant pt is diagnosed with COVID?

- Outpatient monitoring with a 14-day self-quarantine can be considered for pregnant patients with COVID-19 who have mild symptoms or are asymptomatic.
- Clinical judgment, test availability, community spread, and other local policies should be used to decide which patients are tested for SARS-CoV-2.
- Signs and symptoms of COVID-19 range from mild to severe and include fever, myalgias, cough, and difficulty breathing as well as gastrointestinal symptoms and anosmia in some patients.
- The CDC also recommends that depending on case burden and available resources, anyone with a close exposure should be tested immediately after exposure, and if negative, could be tested again about 5-7 days after last exposure or immediately if symptoms develop during quarantine.
- In most adult patients, if dyspnea develops, it tends to occur between 4 and 8 days after symptom onset, although it can also occur after 10 days.

It is recommended that COVID-19 positive patients wear masks at all times and remain isolated, whether outpatient or inpatient, until convalesced, unless not feasible due to clinical care needs.

What that means:

- Frequent phone contact with office RNs (as often as daily if uncertain about progression)
- Consider SARS-Co-V monoclonal ab
- We delay prenatal visits and US if we can to complete the quarantine period (changed to 10 days by CDC)
- If pts need testing we occasionally request to be done in L&D if sufficient isolation can not be done in the office
- Follow growth
- Watch for preeclampsia

SMFM Guidelines, 2020

Pregnant patients should be offered monoclonal antibody infusion if they get COVID

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

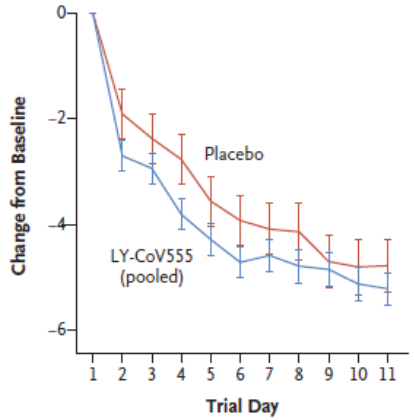
SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

- SARS-CoV-2 gains entry into cells through binding of its spike protein to receptors for angiotensin-converting enzyme 2 on target cells.
- LY-CoV555 (also known as LY3819253), a potent antispike neutralizing monoclonal antibody that binds with high affinity to the receptor-binding domain of SARS-CoV-2, was derived from convalescent plasma obtained from a patient with Covid-19.

N ENGL J MED 384;3 NEJM.ORG JANUARY 21, 2021

Symptom scores were reduced my monoclonal ab administration

Hospitalization:
Day 29, % hospitalized:
Placebo: 6.3%
Antibody: 1.6%



	Delta Value (95% CI)
Day 2	−0.79 (−1.35 to −0.24)
Day 3	−0.57 (−1.12 to −0.01)
Day 4	−1.04 (−1.60 to −0.49)
Day 5	−0.73 (−1.28 to −0.17)
Day 6	−0.79 (−1.35 to −0.23)
Day 7	−0.50 (−1.06 to 0.07)
Day 8	−0.65 (−1.28 to −0.02)
Day 9	−0.15 (−0.75 to 0.45)
Day 10	−0.32 (−0.94 to 0.29)
Day 11	−0.44 (−1.02 to 0.15)

Figure 3. Symptom Scores from Day 2 to Day 11.
Shown is the difference in the change from baseline (delta value) in symptom scores between the LY-CoV555 group and the placebo group from day 2 to day 11. The symptom scores ranged from 0 to 24 and included eight domains, each of which was graded on a scale of 0 (no symptoms) to 3 (severe symptoms). The I bars represent 95% confidence intervals. Details about the symptom-scoring methods are provided in the Supplementary Appendix.

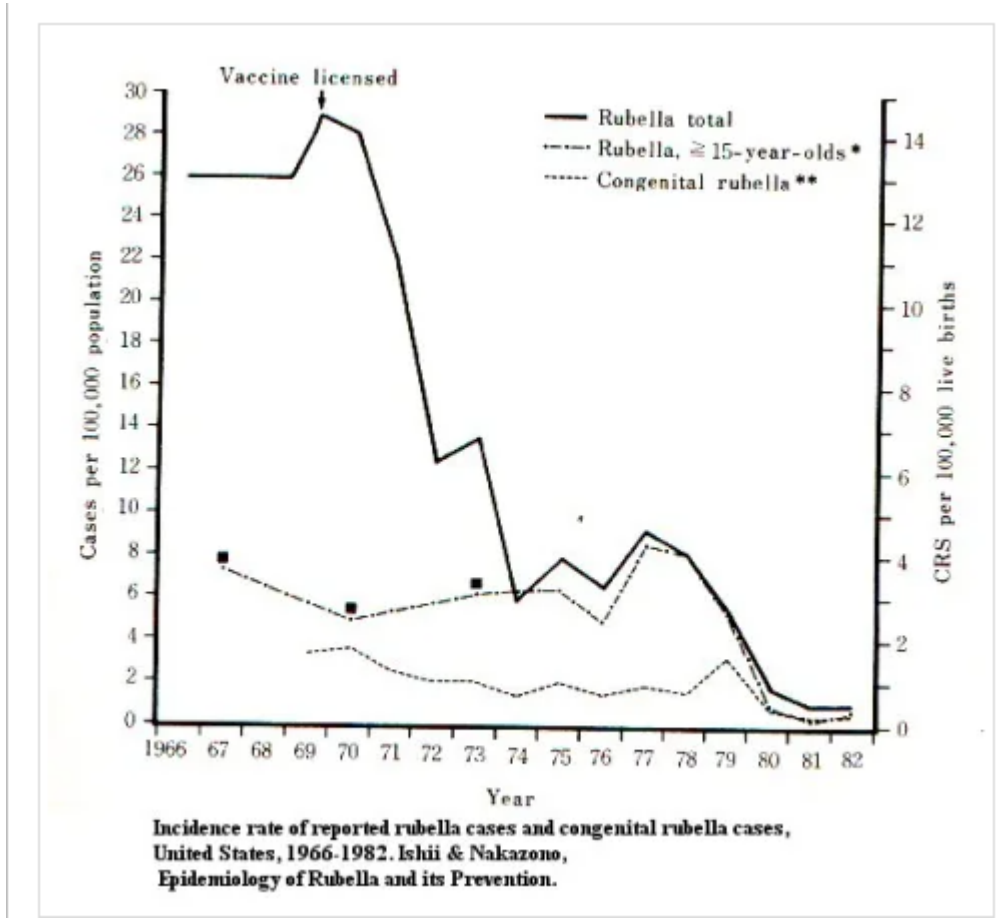
Recommendation (CDC): Post exposure or mild disease (w/in 7 days exposure or 10 days of illness):
The Panel recommends using one of the following anti-SARS-CoV-2 mAbs (listed alphabetically) as PEP for people who are at high risk for progressing to severe COVID-19 if infected with SARS-CoV-2 AND who have the vaccination status AND exposure history outlined in the text below.
• Bamlanivimab 700 mg plus etesevimab 1,400 mg administered as an IV infusion (BIII); or
• Casirivimab 600 mg plus imdevimab 600 mg administered as subcutaneous (SQ) injections (AI) or an IV infusion (BIII).

COVID in pregnancy:
BAD

Vaccine:
Substantial safety and efficacy data
Concerns re: vaccination in pregnancy should be considered in the context of the considerable risk COVID infection in pregnancy portends

Vaccine and Pregnancy

Historically, patients have embraced vaccine to reduce pregnancy risk:
Congenital rubella, once common, now rare



Incidence rate of reported rubella cases and congenital rubella cases, United States, 1966-1982. Ishii & Nakazono, Epidemiology of Rubella and its Prevention.

FIGURE 1. Number of reported rubella and congenital rubella syndrome (CRS) cases, by year — United States, 1980–1996

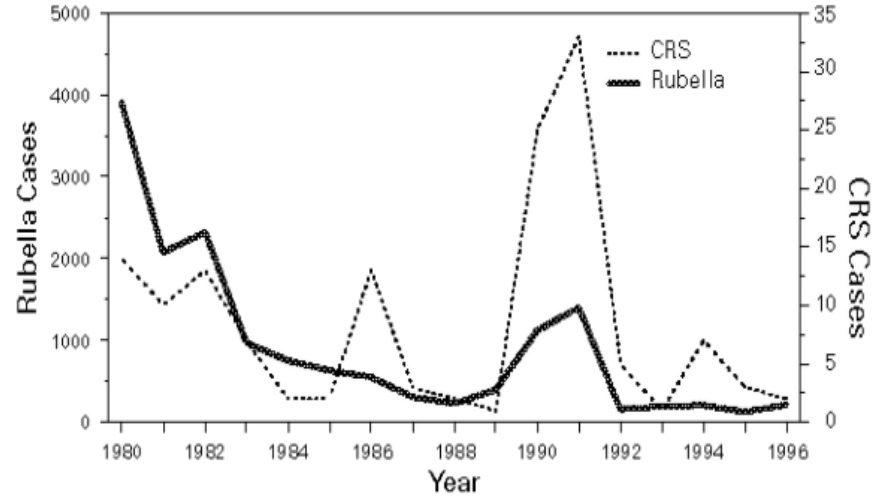
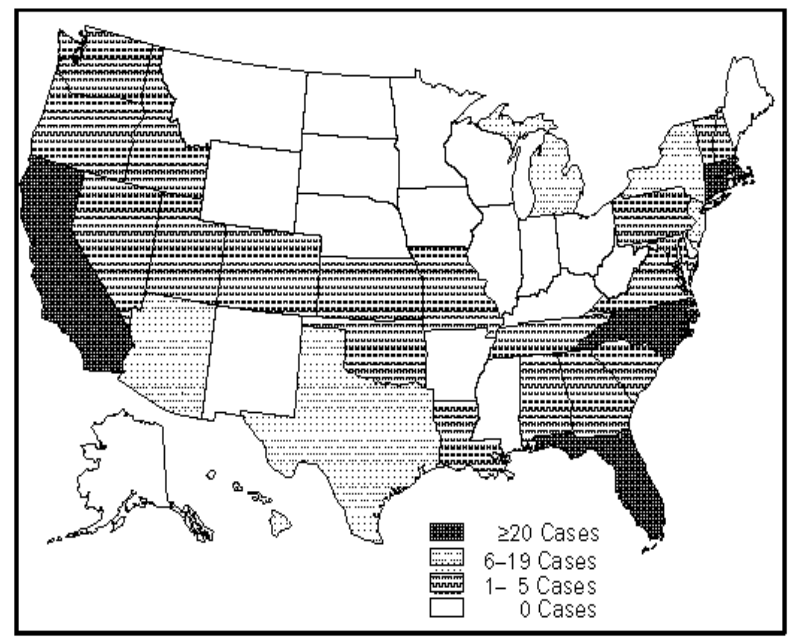


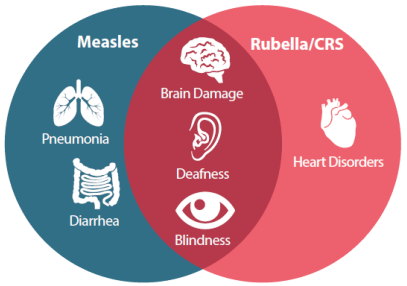
FIGURE 2. Number of reported rubella cases — United States, 1994–1996



[Rubella and CRS | Exploring Vaccines (wordpress.com)]

[Rubella Virus (stanford.edu)]

Outbreaks will occur until vaccination is available and accepted worldwide (note peaks in countries with vaccine available due to low vaccination rates in some areas)



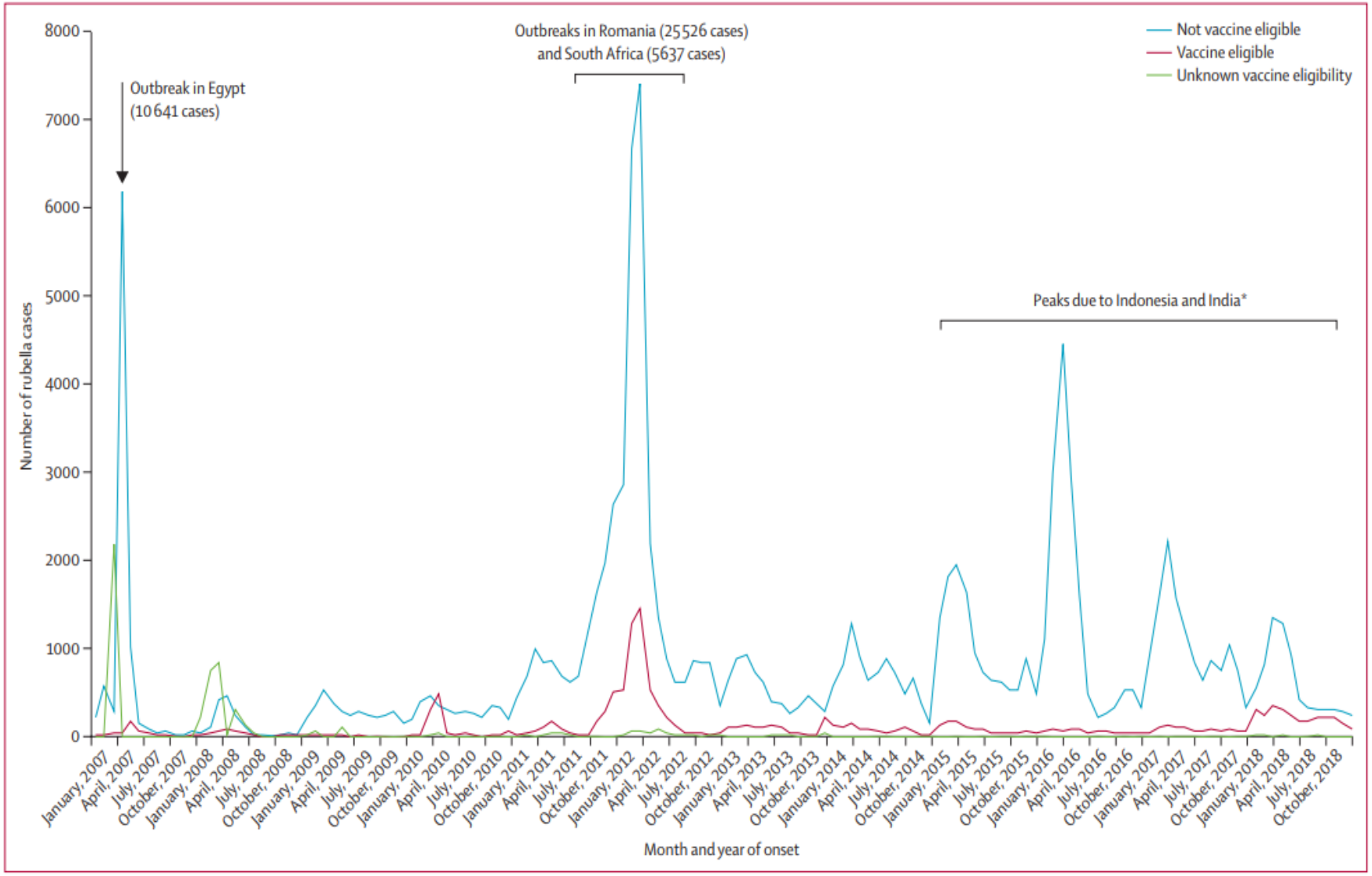


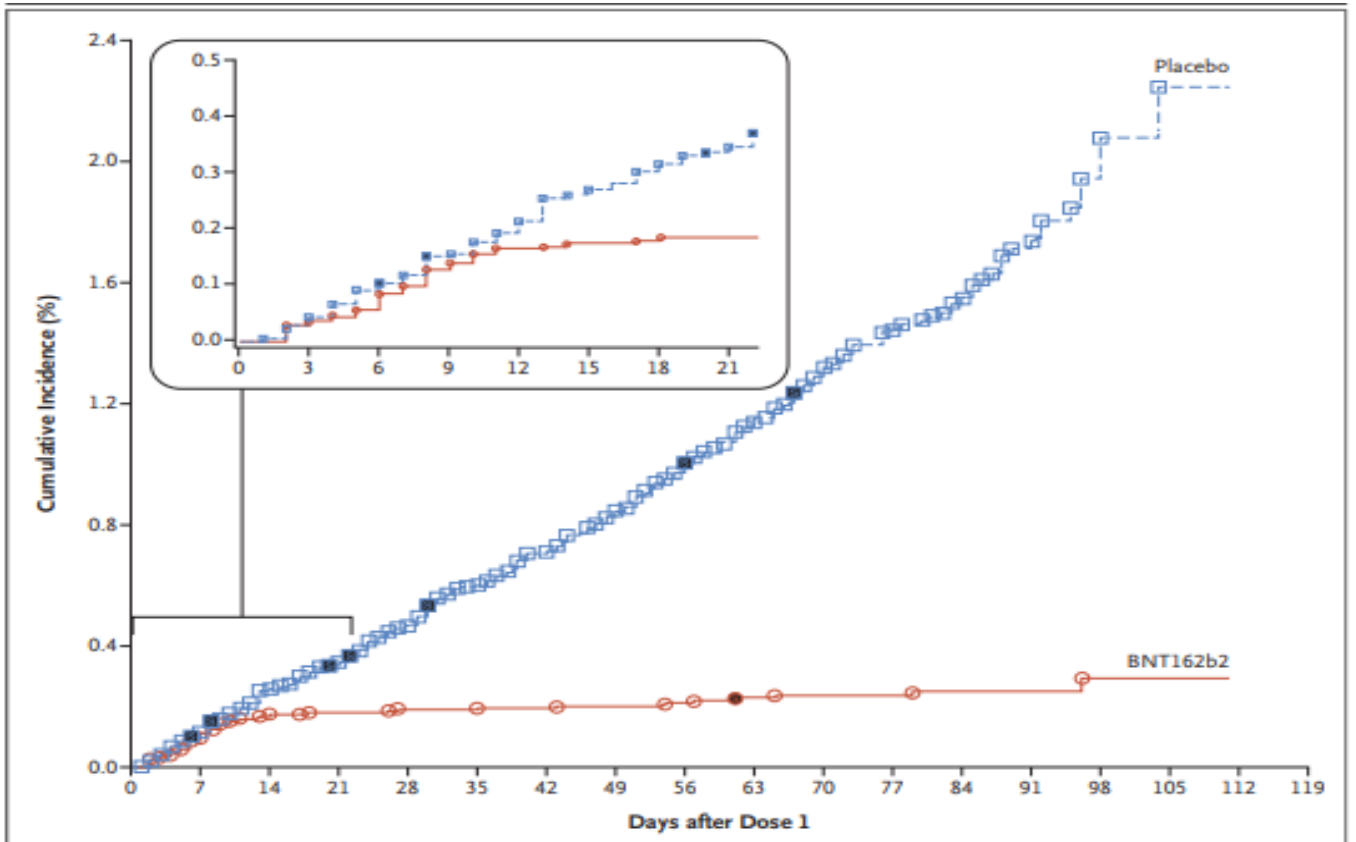
Figure 2: **Reported rubella cases by date of onset and by vaccine eligibility, 2007–18**

*India and Indonesia started reporting rubella cases in 2015.

COVID vaccines work, too

Cumulative incidence of COVID infection after the first dose

(pretty good by the time of second dose)



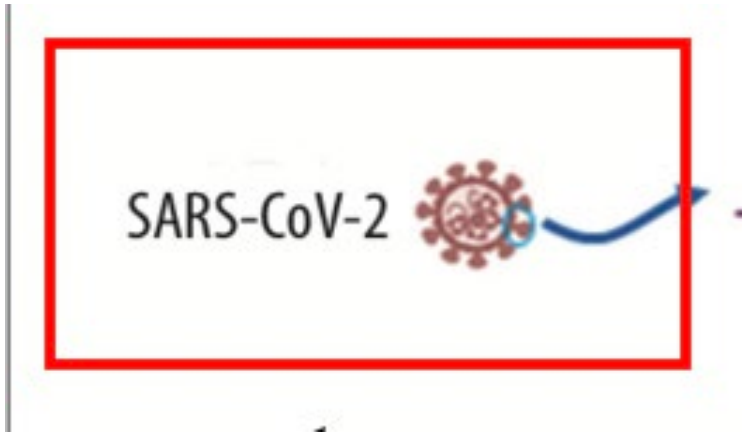
Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time person-yr (no. at risk)	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time person-yr (no. at risk)	VE (95% CI) percent
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

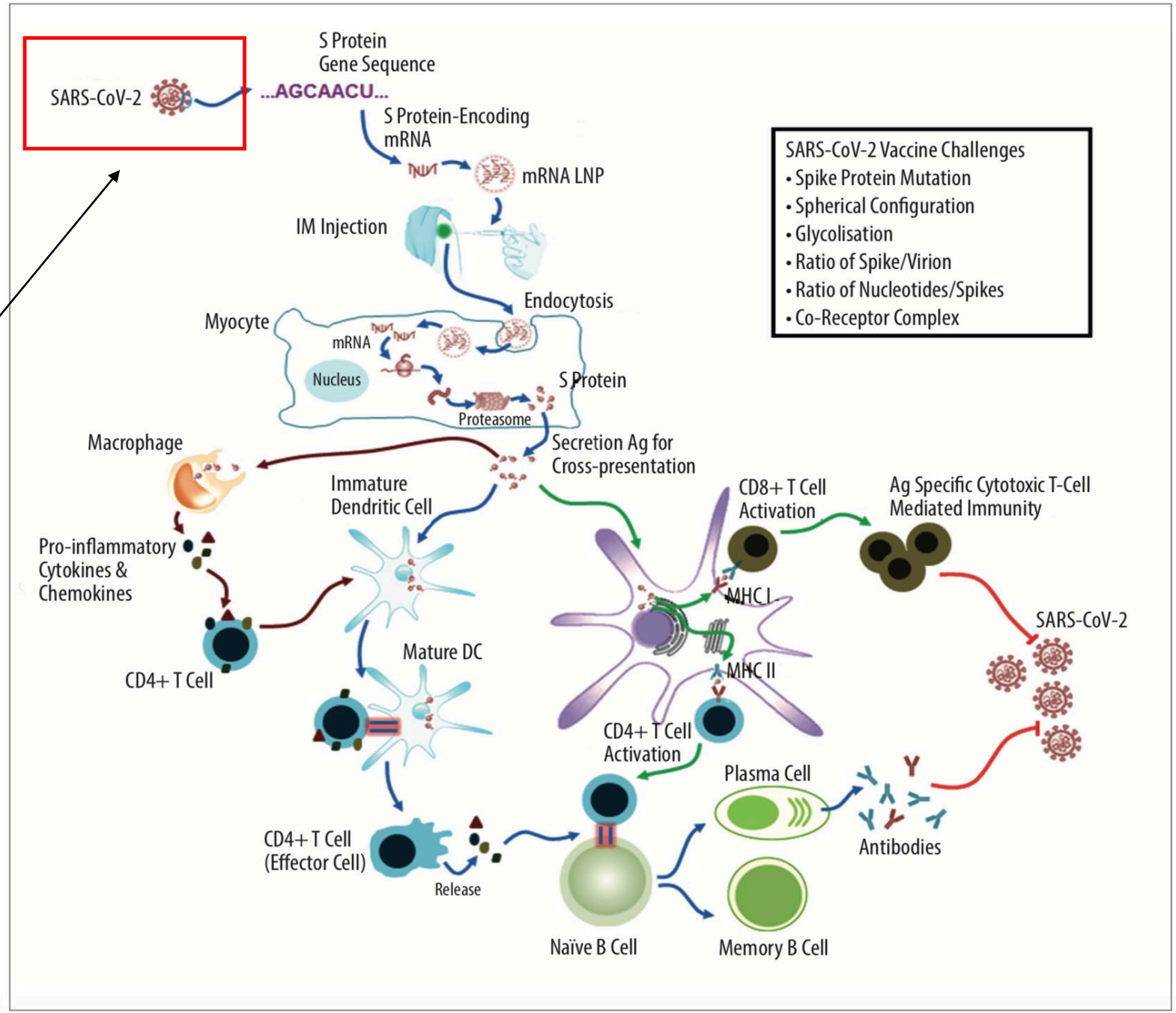
Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.
Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.

DOI: 10.1056/NEJMoa2034577

mRNA vaccines

(1) The main antigen that elicits immunity in native COVID infection is the Spike Protein (S protein). Both cellular (T cells) and humoral (neutralizing antibody) mechanism to this protein is the immunologic response to SARS-CoV2.





Wang F. et al.:
Status of mRNA SARS-CoV-2 vaccines
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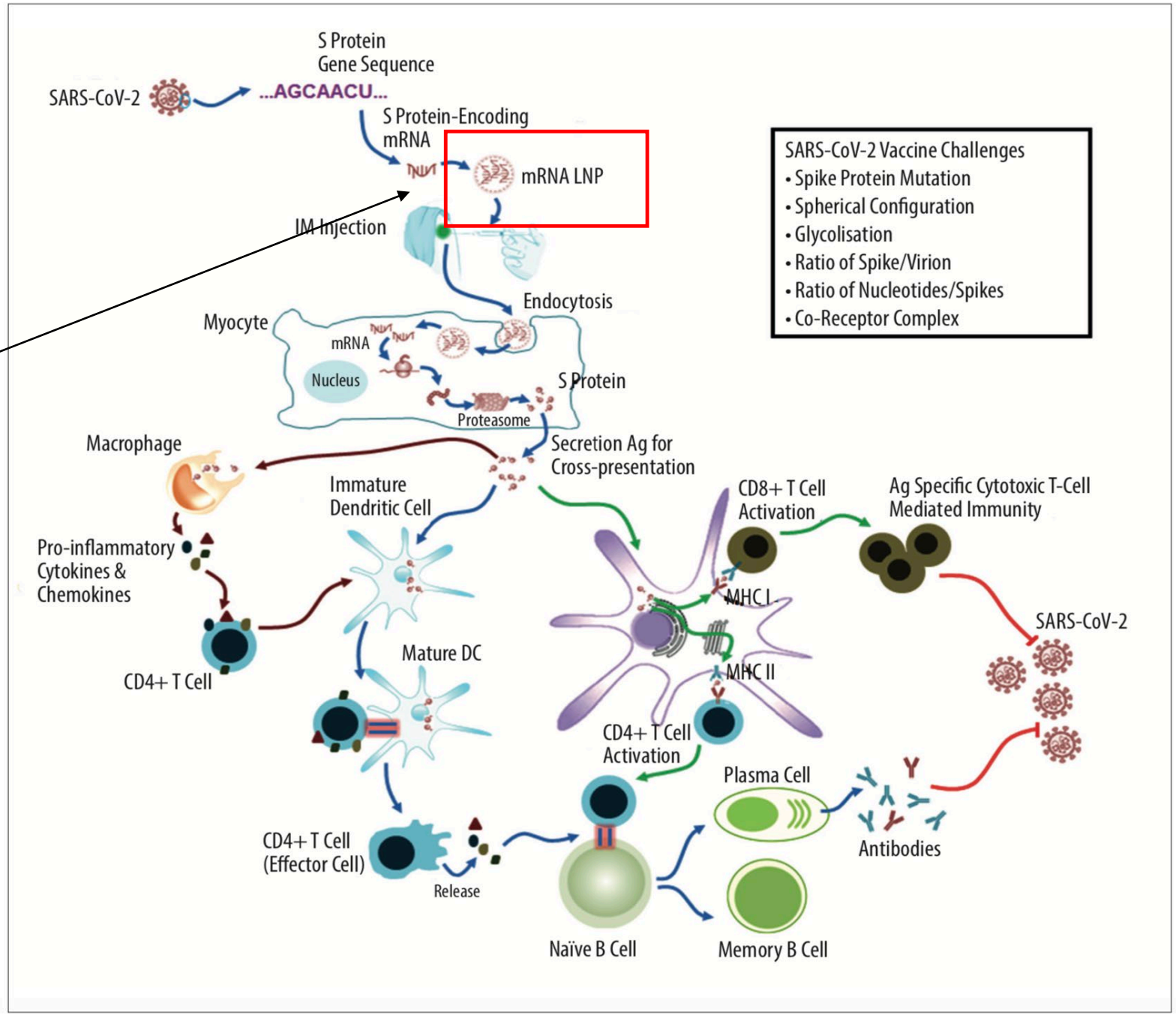
(2) The mRNA to the Spike protein is made and packaged in a lipid nanoparticle



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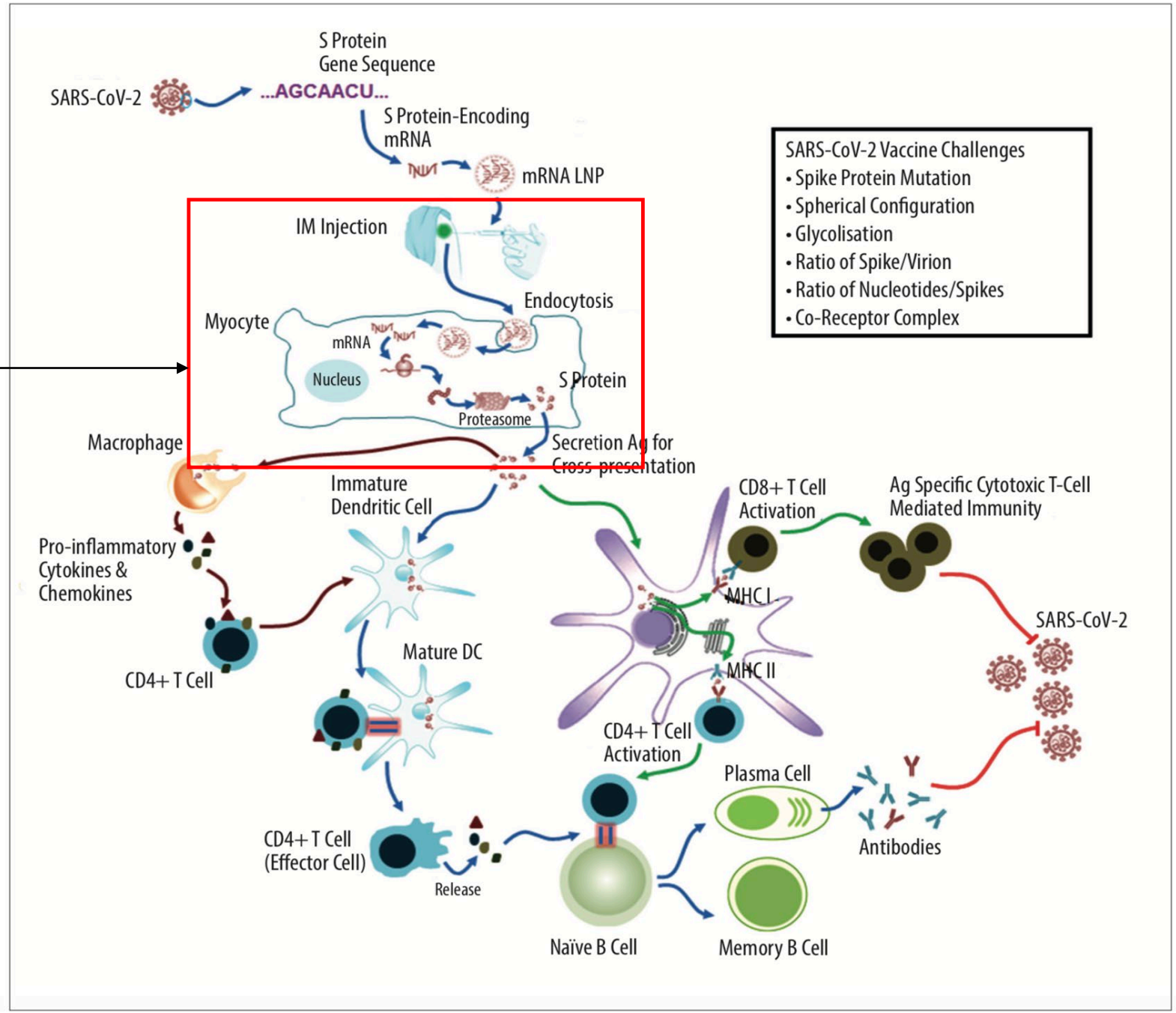
(2) The mRNA to the Spike protein is made and packaged in a lipid nanoparticle for atability and ability for the mRNA to enter the cell

(3) The lipid nanoparticles containing the mRNA is injected IM; the particles enter the myocytes and the same cellular machinery that makes other proteins starts making the Spike protein from the mRNA



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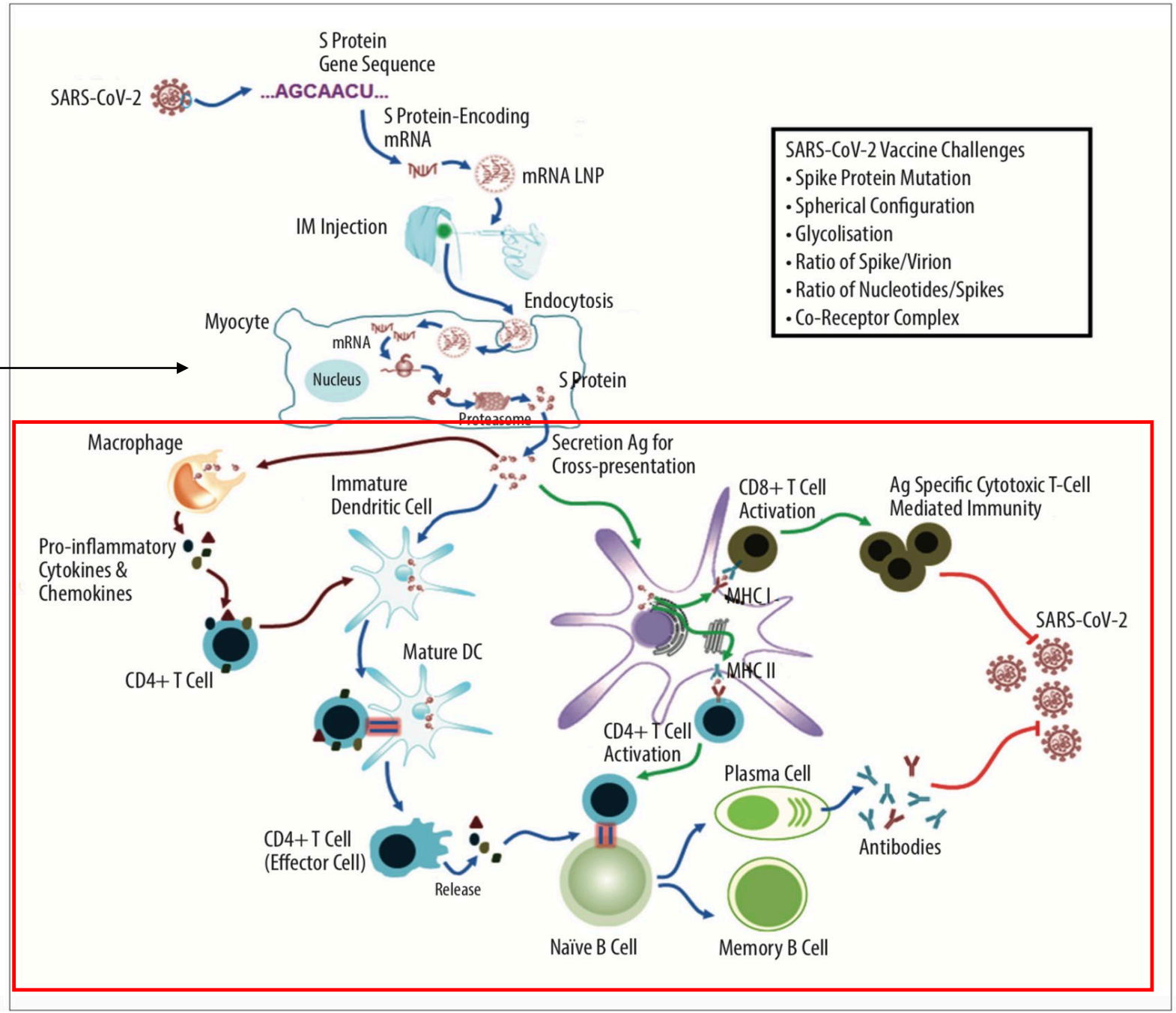
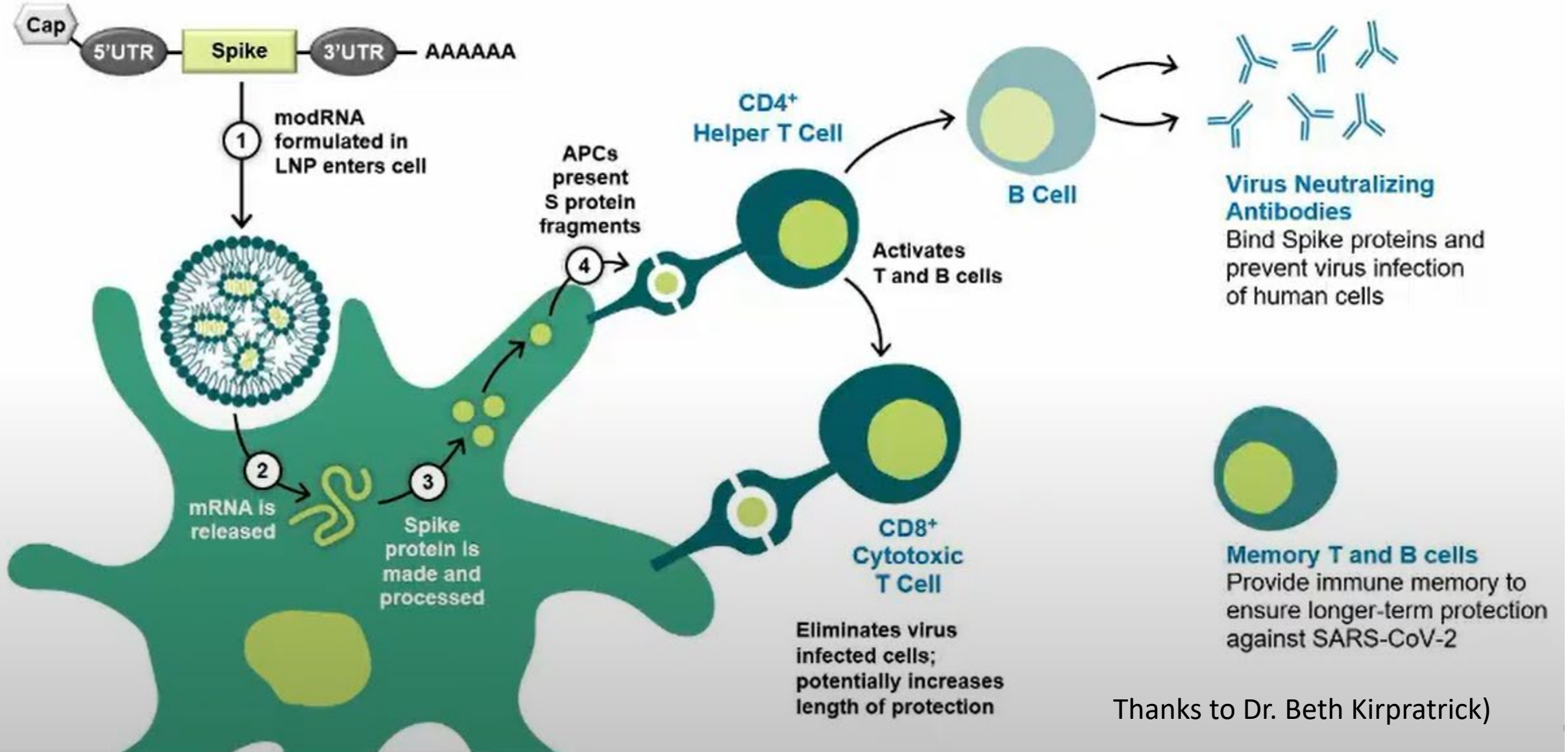
(3) The lipid nanoparticles containing the mRNA is injected IM; the particles enter the myocytes and the same cellular machinery that makes other proteins starts making the Spike protein from the mRNA

(4) The Spike protein is secreted/expressed, identified by the lymphatic system, and the immune system does it magic (ask Liz) to create cellular and humoral immunity



Mode of Action of the BNT162 Vaccine Candidates

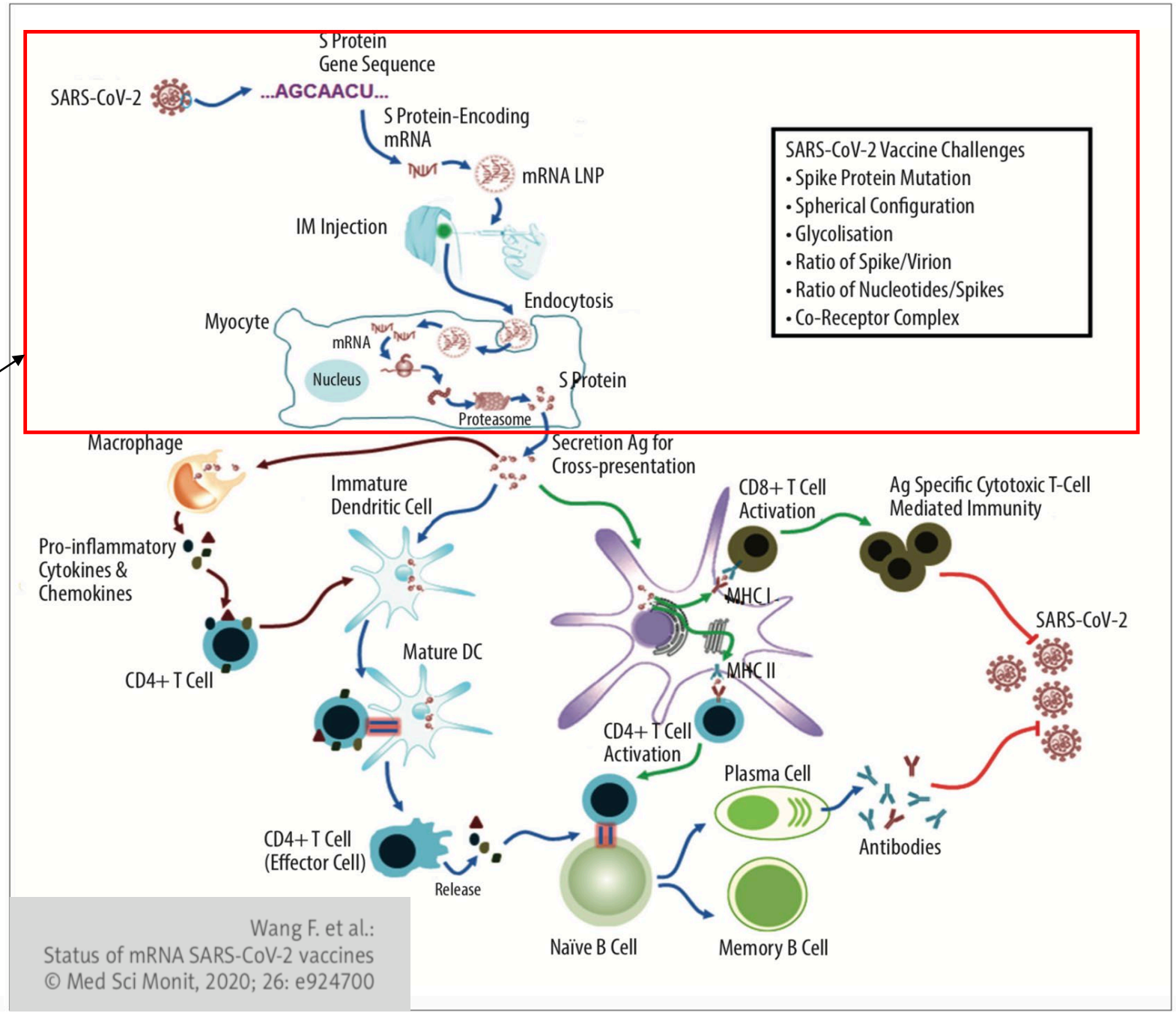


Thanks to Dr. Beth Kirpratrick)

mRNA vaccines:

Noteworthy characteristics

(1) mRNA is not stable and is naturally degraded in the cell when transcription job is done (days)
(2) mRNA does not enter the nucleus and does not interact with DNA (no risk of insertional mutation, an issue with DNA based vaccines)
(3) mRNA is NOT infectious
(4) ***Given how mRNA vaccines act locally (at the site of injection) and are rapidly degraded and removed by lymphatic system, it is unlikely that the vaccine would reach and cross the placenta (G. Swamy, MD, SMFM)***



mRNA vaccines:

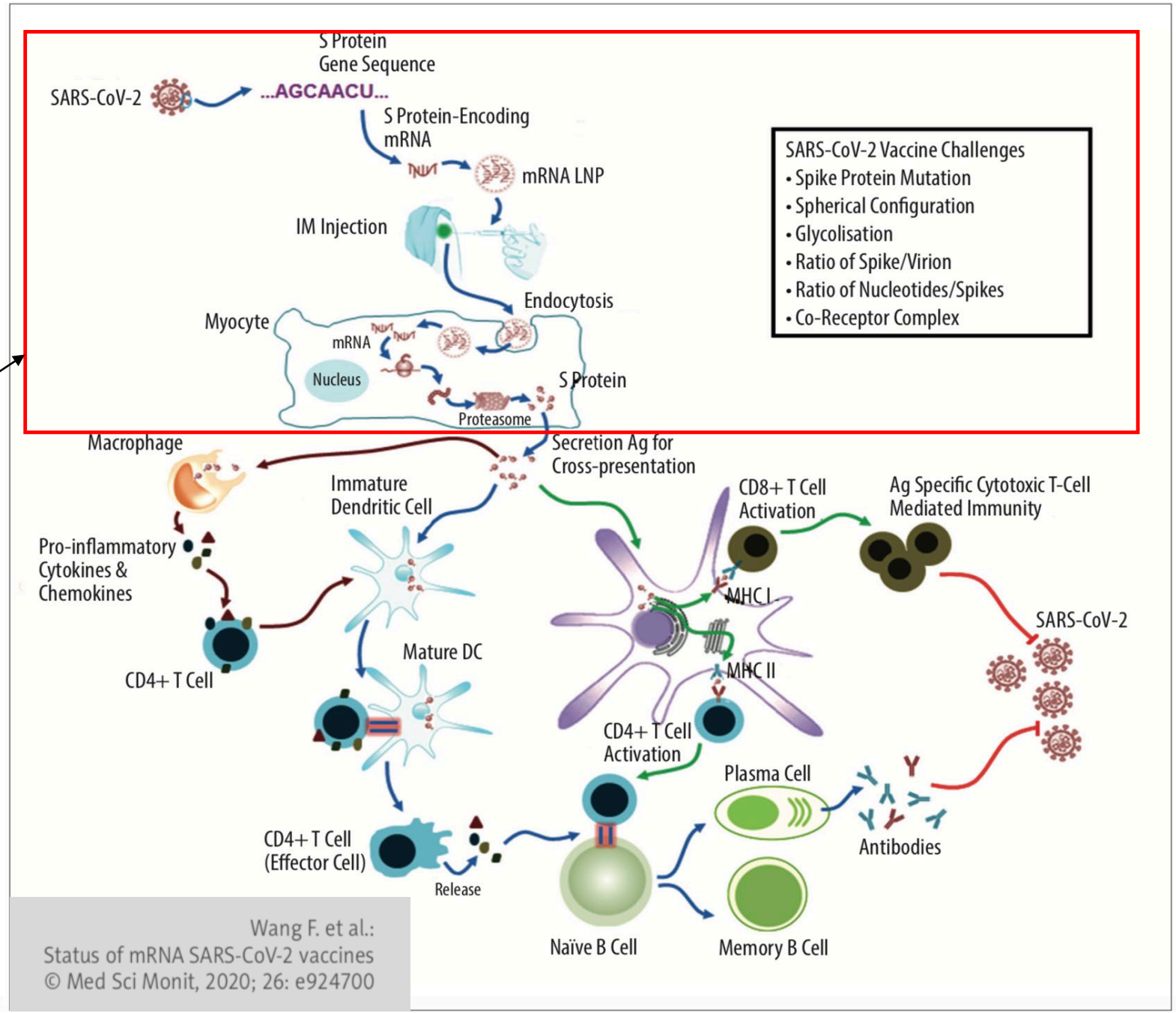
Biologic Plausibility of placental interaction and effect of immune activation to COVID

(1) mRNA is not stable and is a large molecule with a negative charge: even if it makes it to the placental interface, the biochemical characteristics suggest it would not cross the placental interface

(2) Even if a lipid nanoparticle made the way to placenta, it might make Spike antigen and then stop just as the myocytes

(3) The immune response to pregnant pts with covid and the vaccine are very similar: Ab and T cell response to the Spike protein. We know pregnant infected women are sick but no evidence that the immune response is harmful to mom or baby (and potential passive immunity). No biologic reason to think the antigen would be worse than the viral effects-which are largely related to maternal disease not the virus per se

(4) We DO know preterm birth and maternal illness are bad



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., Ashley N. Smoots, M.P.H., Caitlin J. Green, M.P.H., Charles Licata, Ph.D., Bicheng C. Zhang, M.S., Meghna Alimchandani, M.D., Adamma Mba-Jonas, M.D., Stacey W. Martin, M.S., Julianne M. Gee, M.P.H., and Dana M. Meaney-Delman, M.D., for the CDC v-safe COVID-19 Pregnancy Registry Team*

COVID vaccine is safe in pregnancy with similar local effects

This article was published on April 21, 2021, at NEJM.org.

Table 2. Frequency of Local and Systemic Reactions Reported on the Day after mRNA Covid-19 Vaccination in Pregnant Persons.*

Reported Reaction	Pfizer–BioNTech Vaccine		Moderna Vaccine		Total	
	Dose 1 (N=9052)	Dose 2 (N=6638)	Dose 1 (N=7930)	Dose 2 (N=5635)	Dose 1 (N=16,982)	Dose 2 (N=12,273)
	number (percent)					
Injection-site pain	7602 (84.0)	5886 (88.7)	7360 (92.8)	5388 (95.6)	14,962 (88.1)	11,274 (91.9)
Fatigue	2406 (26.6)	4231 (63.7)	2616 (33.0)	4541 (80.6)	5,022 (29.6)	8,772 (71.5)
Headache	1497 (16.5)	3138 (47.3)	1581 (19.9)	3662 (65.0)	3,078 (18.1)	6,800 (55.4)
Myalgia	795 (8.8)	2916 (43.9)	1167 (14.7)	3722 (66.1)	1,962 (11.6)	6,638 (54.1)
Chills	254 (2.8)	1747 (26.3)	442 (5.6)	2755 (48.9)	696 (4.1)	4,502 (36.7)
Fever or felt feverish	256 (2.8)	1648 (24.8)	453 (5.7)	2594 (46.0)	709 (4.2)	4,242 (34.6)
Measured temperature ≥38°C	30 (0.3)	315 (4.7)	62 (0.8)	664 (11.8)	92 (0.5)	979 (8.0)
Nausea	492 (5.4)	1356 (20.4)	638 (8.0)	1909 (33.9)	1,130 (6.7)	3,265 (26.6)
Joint pain	209 (2.3)	1267 (19.1)	342 (4.3)	1871 (33.2)	551 (3.2)	3,138 (25.6)
Injection-site swelling	318 (3.5)	411 (6.2)	739 (9.3)	1051 (18.7)	1,057 (6.2)	1,462 (11.9)
Abdominal pain	117 (1.3)	316 (4.8)	160 (2.0)	401 (7.1)	277 (1.6)	717 (5.8)
Injection-site redness	160 (1.8)	169 (2.5)	348 (4.4)	491 (8.7)	508 (3.0)	660 (5.4)
Diarrhea	178 (2.0)	277 (4.2)	189 (2.4)	332 (5.9)	367 (2.2)	609 (5.0)
Vomiting	82 (0.9)	201 (3.0)	77 (1.0)	357 (6.3)	159 (0.9)	558 (4.5)
Injection-site itching	103 (1.1)	109 (1.6)	157 (2.0)	193 (3.4)	260 (1.5)	302 (2.5)
Rash	20 (0.2)	18 (0.3)	22 (0.3)	18 (0.3)	42 (0.2)	36 (0.3)

* Shown are solicited reactions in v-safe participants 16 to 54 years of age who identified as pregnant and who received an mRNA Covid-19 vaccine (BNT162b2 [Pfizer–BioNTech] or mRNA-1273 [Moderna]) from December 14, 2020, to February 28, 2021.

COVID vaccine is safe in pregnancy with pregnancy outcomes similar to background rates in pregnancy

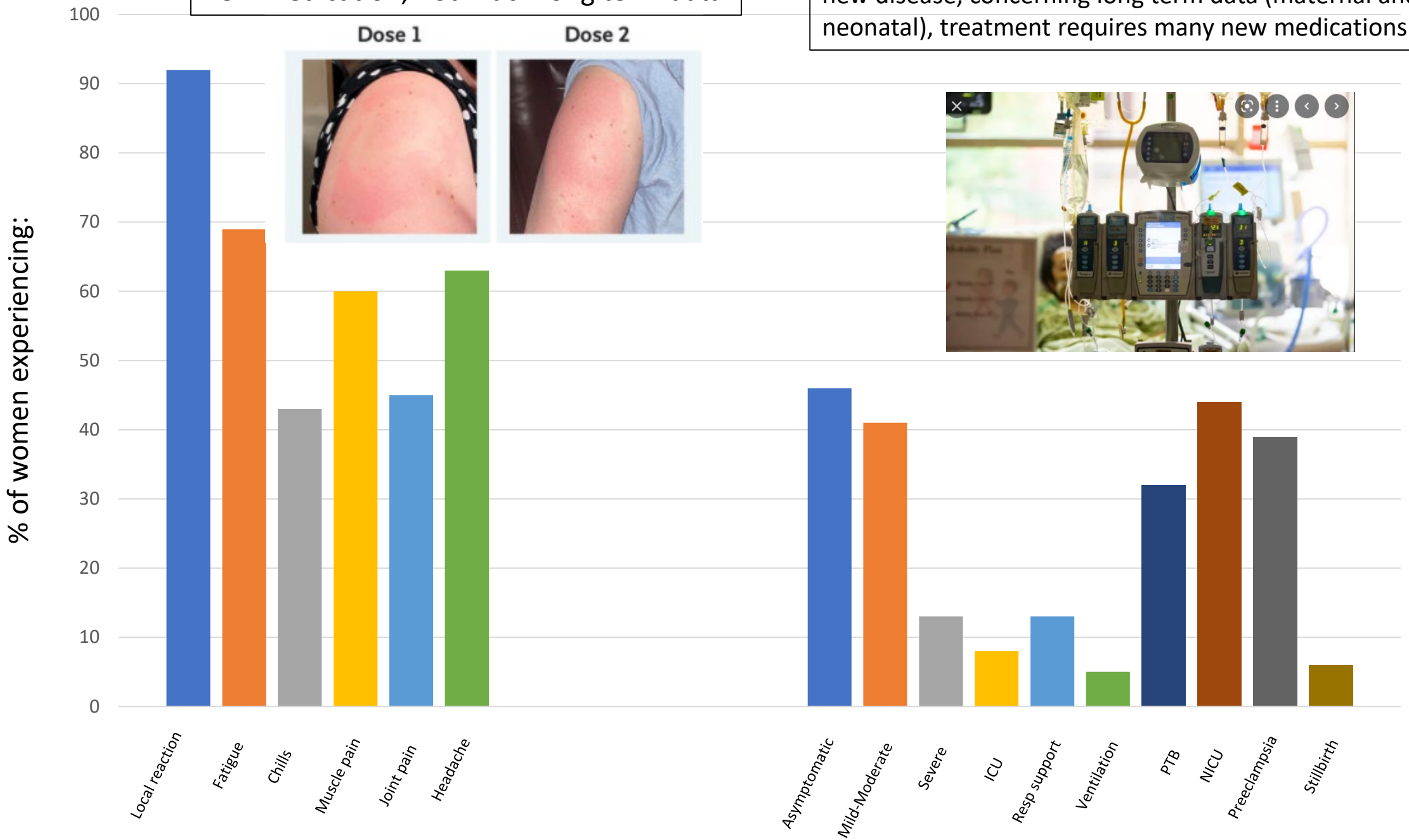
Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	*no./total no. (%)*
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk[15-17]	10–26	104/827 (12.6)‡
Stillbirth: ≥ 20 wk[18-20]	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk[21,22]	8–15	60/636 (9.4)¶
Small size for gestational age[23,24]‖	3.5	23/724 (3.2)
Congenital anomalies[25]**	3	16/724 (2.2)
Neonatal death[26]††	<1	0/724

This article was published on April 21, 2021, at NEJM.org.

COVID Vaccine Effects in pregnancy:
new medication, not much long term data

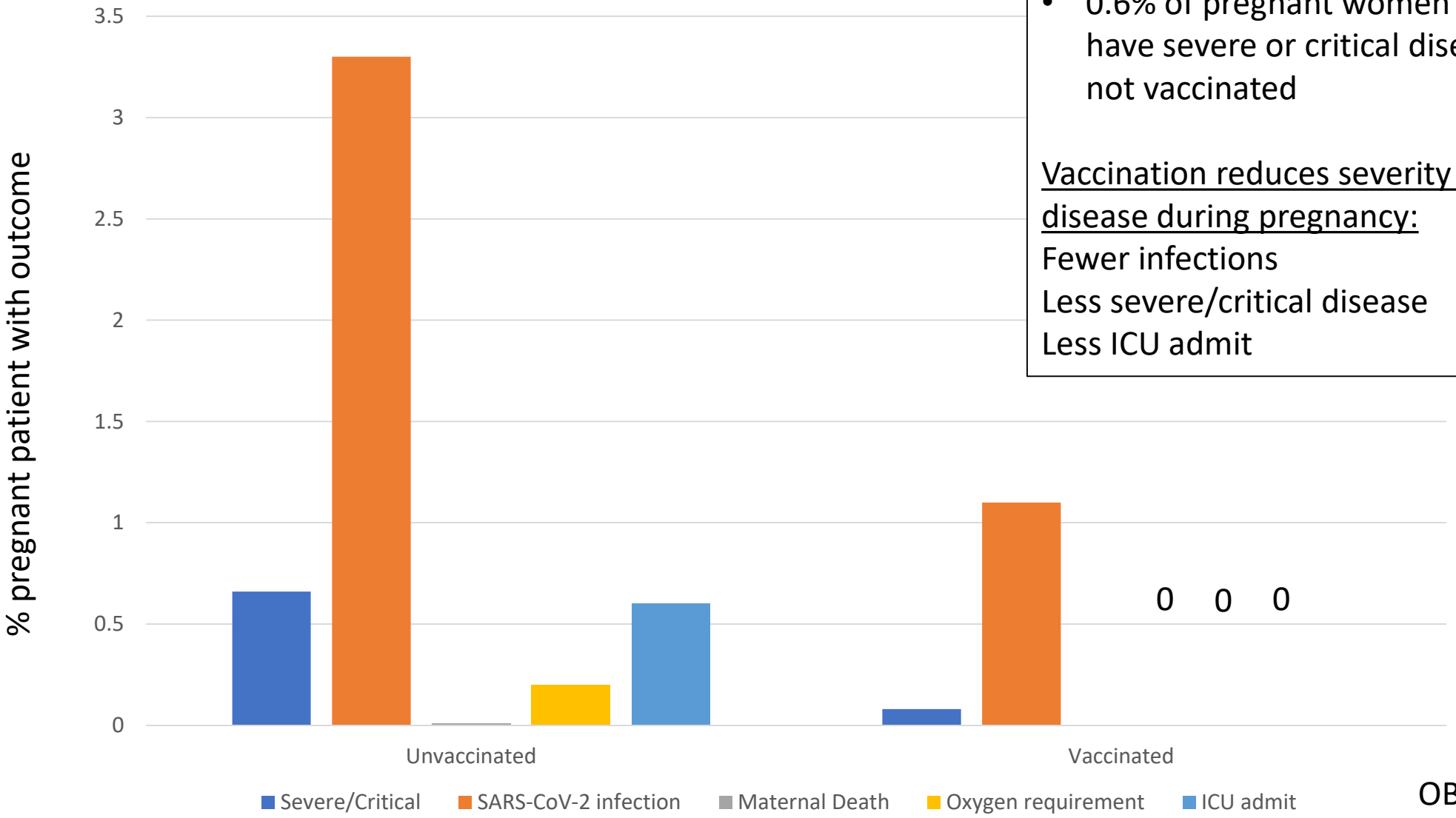
COVID Infection Effects in pregnancy:
new disease, concerning long term data (maternal and neonatal), treatment requires many new medications



COVID infection is dangerous for pregnant women:
Covid vaccination reduces severity of infection

- 3% of pregnant women will get Covid if not vaccinated
- 0.6% of pregnant women will have severe or critical disease if not vaccinated

<u>Vaccination reduces severity of disease during pregnancy:</u>
Fewer infections
Less severe/critical disease
Less ICU admit



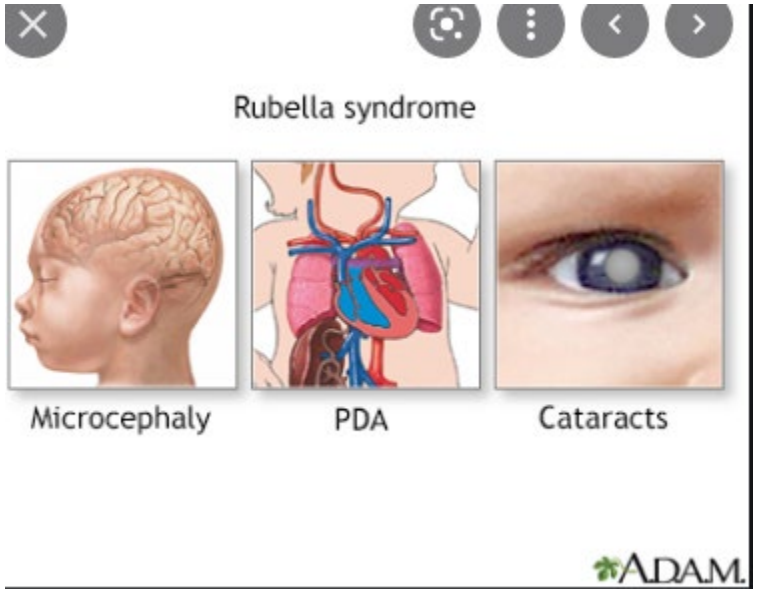
OBGYN, epub 10/2021

Does COVID vaccine development use fetal tissue?

- Cell lines derived from aborted fetal tissue have been fairly commonplace in research and medicine since the creation in the 1960s of the WI-38 cell strain, which was derived at the Wistar Institute in Philadelphia, Pennsylvania, and MRC-5, which came from a Medical Research Council laboratory in London (see *Nature* **498,** 422–426; 2013).
- These same lines are used today (current use are from cell lines isolated in 1960s)
- Viruses multiply readily in these cells, and they are used to manufacture many globally important vaccines:
  - measles, rubella, rabies, chicken pox, shingles and hepatitis A
  - The J&J Covid vaccine does involve incubation of virus in fetal retinal cells
  - The mRNA vaccines used fetal cells early in the vaccine research but does not use fetal cells in the manufacture of vaccine

Nature 2015

Rubella vaccine:
Incubated in fetal cells
Reduces the risk of congenital rubella



- Before 11 WG, the congenital infection rate approaches 90%, decreases to 30% between 24 and 26 WG and increases to nearly 100% beyond 36 WG
- Infection in the first 12 WG, the risk of major fetal defects nears 85%, with approximately 20% of the cases resulting in spontaneous abortions in the first 8 WG
- An estimated 20,000 cases of CRS occurred during 1964-1965 during the last U.S. rubella epidemic before rubella vaccine became available
- Since monovalent vaccines containing measles, rubella, and mumps vaccine viruses -- and subsequently combined measles-mumps-rubella (MMR) vaccine -- were licensed, the numbers of reported cases of measles, mumps, rubella, and congenital rubella syndrome (CRS) have decreased by more than 99%.
- Mandated Vaccination:
  - In 1977, ACIP modified its recommendations to include the vaccination of susceptible postpubertal girls and women. During the same year, the DHEW undertook the National Childhood Immunization Initiative, which sought to immunize greater than 90% of the nation's children against all vaccine-preventable diseases. Enforcement of requirements for vaccination before school entry was part of the initiative.
  - The number of reported rubella and CRS cases decreased after these programs were implemented, from 20,395 rubella cases and 29 CRS cases in 1977 to 752 rubella cases and 2 CRS cases in 1984. In 1988, 225 cases of rubella were reported in the United States, the fewest since national reporting began.

About 30% of deafness worldwide is due to viral infection, largely rubella (Brazil: 32%)

1989 study:
Of 242 college students with deafness, 104 were due to congenital to rubella

Prenatal Diagnosis 2014, 34, 1246–1253

CDC MMWR: May 22, 1998:

Does Covid19 vaccination cause infertility?

No

Here's Where That COVID-19 Vaccine Infertility Myth Came From—And Why It Is Not True

Posted on April 23, 2021 by ***Henry Ford Health System Staff*** 585862 Share

Last December, a German epidemiologist said the COVID-19 vaccines might make women's bodies reject a protein that's connected to placenta, therefore making women infertile. He thought this because the genetic code of the placenta protein, called syncytin-1, shares a hint of similarity with the genetic code of the spike protein in COVID-19. If the vaccines caused our bodies to make antibodies to protect us from COVID-19, he thought, they could also make antibodies to reject the placenta.

This, however, was a theoretical risk that was completely disproven in the clinical trials and continues to be disproven in real time as more women of child-bearing age become fully vaccinated.

[Here's Where That COVID-19 Vaccine Infertility Myth Came From—And Why It Is Not True | Henry Ford LiveWell]

ELSEVIER

F&S Reports

Volume 2, Issue 3, September 2021, Pages 253-255

Special contribution

SARS-CoV-2 spike protein seropositivity from vaccination or infection does not cause sterility

Randy S. Morris M.D.

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https://doi.org/10.1016/j.xfre.2021.05.010

Several reports claim that the purported similarity between syncytin-1 and the SARS-CoV-2 spike protein may induce immune cross-reactivity resulting in female sterility. We used frozen embryo transfer as a model for comparing the implantation rates between SARS-CoV-2 vaccine seropositive, infection seropositive, and seronegative women. No difference was found in serum hCG documented implantation rates or sustained implantation rates between the three groups. Reports claiming that COVID-19 vaccines or illness cause female sterility are unfounded.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage

Does getting the COVID vaccine cause miscarriage? No

- COVID Vaccine does not increase risk of first trimester SAB:
- Case: pts with SAB <14 weeks
- Control: Ongoing pregnancy
- Exposure: COVID vaccine in 5-week or 3-week window of SAB or ongoing pregnancy
- Adjustment: age, marital status, country of origin, education, income, number of children, employment

Table 1. Odds Ratios for Covid-19 Vaccination in a 5-Week or 3-Week Window before Miscarriage or Confirmation of an Ongoing Pregnancy.

Vaccination Status	5-Week Exposure Window				3-Week Exposure Window			
	Ongoing Pregnancies	Miscarriages	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*	Ongoing Pregnancies	Miscarriages	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*
	number				*number*			
Among all women								
Unvaccinated	13,184	4,290	Reference	Reference	13,507	4,375	Reference	Reference
Vaccinated	772	231	0.92 (0.79–1.07)	0.81 (0.69–0.95)	449	146	1.00 (0.83–1.21)	0.91 (0.75–1.10)
Among health care personnel								
Unvaccinated	2,419	756	Reference	Reference	2,533	788	Reference	Reference
Vaccinated	261	75	0.92 (0.70–1.20)	0.93 (0.70–1.22)	147	43	0.94 (0.66–1.33)	0.92 (0.64–1.32)

* The odds ratios among all women were adjusted for age, country of birth, marital status, educational level, household income, number of children, employment in a health care profession, underlying risk conditions for coronavirus disease 2019 (Covid-19), and previous test positive for severe acute respiratory syndrome coronavirus 2. The odds ratios among health care personnel were adjusted for the same variables as among all women except for employment in a health care profession.

This letter was published on October 20, 2021, at NEJM.org.

ORIGINAL ARTICLE

Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

D. Mevorach, E. Anis, N. Cedar, M. Bromberg, E.J. Haas, E. Nadir, S. Olsha-Castell, D. Arad, T. Hasin, N. Levi, R. Asleh, O. Amir, K. Meir, D. Cohen, R. Dichtiar, D. Novick, Y. Hershkovitz, R. Dagan, I. Leitersdorf, R. Ben-Ami, I. Miskin, W. Saliba, K. Muhsen, Y. Levi, M.S. Green, L. Keinan-Boker, and S. Alroy-Preis

I do not want vaccination since it can hurt my heart….

Mostly young males

(Pfizer)

Table 1. Reported Myocarditis Cases, According to Timing of First or Second Vaccine Dose.*

Timing	First Vaccine Dose			Second Vaccine Dose			Both Doses
	No. of Vaccinations	Myocarditis Cases	Males/ Females	No. of Vaccinations	Myocarditis Cases	Males/ Females	Myocarditis Cases
Six-month study period	5,442,696	19	17/2	5,125,635	117	101/16	136
December 2020	987,013	0	0/0	0	0	0/0	0
January 2021	2,109,854	4	3/1	1,844,896	13	12/1	17
February 2021	1,613,909	6	5/1	1,546,184	47	41/6	53
March 2021	528,069	7	7/0	1,397,609	44	38/6	51
April 2021	152,765	1	1/0	253,701	13	10/3	14
May 2021	51,086	1	1/0	83,245	0	0	1

* Data are from medical records, including clinical and laboratory data and discharge summaries, from the Ministry of Health database from December 2020 through May 2021, according to the codes for myocarditis used in the *International Classification of Diseases, 9th Revision*. Cases of myocarditis were reported within 21 days after the first dose of vaccine and 30 days after the second dose. All cases were clinically reviewed, and only definite or probable cases are shown.

This article was published on October 6, 2021, at NEJM.org.

Table 3. Risk of Myocarditis within 21 Days after the First or Second Dose of Vaccine, According to Age and Sex.*

Age and Sex	First Dose			Second Dose			Risk Difference (95% CI)
	Recipients	Cases	Risk per 100,000 Persons	Recipients	Cases	Risk per 100,000 Persons	
	number			*number*			*no./100,000 persons*
Male recipients							
All ages	2,668,894	17	0.64	2,507,210	96	3.83	3.19 (2.37 to 4.02)
16–19 yr	224,518	3	1.34	199,115	30	15.07	13.73 (8.11 to 19.46)
20–24 yr	261,741	5	1.91	239,396	26	10.86	8.95 (4.42 to 13.55)
25–29 yr	246,638	3	1.22	228,988	16	6.99	5.77 (2.02 to 9.58)
30–39 yr	491,126	2	0.41	461,044	17	3.69	3.28 (1.41 to 5.18)
40–49 yr	458,268	3	0.65	433,069	5	1.15	0.50 (−0.82 to 1.84)
≥50 yr	986,603	1	0.10	945,598	2	0.21	0.11 (−0.29 to 0.52)
Female recipients							
All ages	2,773,802	2	0.07	2,618,425	12	0.46	0.39 (0.10 to 0.68)
16–19 yr	219,460	0	0	199,706	2	1.00	1.00 (−0.63 to 2.72)
20–24 yr	250,556	0	0	231,960	5	2.16	2.16 (0.13 to 4.24)
25–29 yr	235,575	0	0	219,113	0	0	0 (−0.83 to 0.89)
30–39 yr	481,045	0	0	451,791	1	0.22	0.22 (−0.37 to 0.84)
40–49 yr	472,083	1	0.21	444,916	2	0.45	0.24 (−0.61 to 1.11)
≥50 yr	1,115,083	1	0.09	1,070,939	2	0.19	0.10 (−0.26 to 0.46)

* Among vaccine recipients of all ages and both sexes, the overall difference in the incidence of myocarditis after the second dose as compared with the incidence after the first dose was 1.76 (95% confidence interval [CI], 1.33 to 2.19). The widths of the confidence intervals have not been adjusted for multiple testing.

<u>Myocarditis:</u>

Risk in highest risk group of young men: 14/100,000 people being vaccinated

<u>Covid infection young adults (18-34):</u>

- ICU 21%
- Ventilator 10%
- Death 2.7%

<u>Covid infection Adolescent (12-17):</u>

- Cumulative hospitalization rate 50/100000 people
- ICU 30%
- Ventilator 5%
- Death 0 (200 cases)

MMWR, June 2021

Decision Tool (not validated but pretty good)

I'm pregnant. Should I get the COVID vaccine?

For most people, getting the COVID vaccine as soon as possible is the safest choice.

However, trials testing the vaccine in pregnant and breastfeeding women have not been completed.

The information below will help you make an informed choice about whether to get the COVID vaccine while you are pregnant or trying to get pregnant.

Your options:

Get the COVID vaccine as soon as it is available

Wait for more information about the vaccine in pregnancy

What are the benefits of getting the COVID Vaccine?

1. COVID is dangerous. It is *more* dangerous for pregnant women.

- COVID patients who are pregnant are 5 times more likely to end up in the intensive care unit (ICU) or on a ventilator than COVID patients who are not pregnant.[1]
- Preterm birth may be more common for pregnant women with severe COVID, but other obstetric complications such as stillbirth do not appear to be increased.[2]
- Pregnant women are more likely to die of COVID than non-pregnant women with COVID who are the same age.[3,4]

2. The COVID vaccine will prevent 95% of COVID infections.

- As COVID infections go up in our communities, your risk of getting COVID goes up too.
- Getting the vaccine will prevent you from getting COVID and will help keep you from giving COVID to people around you.

3. The COVID vaccine cannot give you COVID.

- The COVID vaccine has no live virus.[5]
- The COVID vaccine does NOT contain ingredients that are known to be harmful to pregnant women or to the fetus.
- Many vaccines are routinely given in pregnancy and are safe (for example: tetanus, diphtheria, and flu).

More details about how the vaccine works can be found on page 5.

What are the risks of getting the COVID vaccine?

1. The COVID vaccine has not yet been tested in pregnant women.

- The vaccine was tested in over 20,000 people, and there were no serious side effects. However, it was not tested in pregnant women.
- We do not have data on whether the vaccine works as well in pregnancy as it did in the study of non-pregnant individuals.
- We do not have data on whether there are unique downsides in pregnancy, like different side effects or an increased risk of miscarriage or fetal abnormalities.

2. People getting the vaccine will probably have some side effects.

- Although there were no serious side effects reported, many people had some side effects. The side effects of the vaccine were:
  - injection site reactions like sore arm (84%)
  - fatigue (62%)
  - headache (55%)
  - muscle pain (38%)
  - chills (32%)
  - joint pain (24%)
  - fever (14%)
- About 1% of people will get a high fever (over 102°F). A persistent high fever during the first trimester of pregnancy might increase the risk of congenital defects or miscarriage. For those reasons, you may choose to delay your COVID vaccine until after the first trimester.
- The CDC recommends using Tylenol (acetaminophen) during pregnancy if you have a high fever.

What do the experts recommend?

COVID is very dangerous and can spread very easily. Because of this, ***"the Pfizer-COVID vaccine is recommended for persons 16 years of age and older in the U.S. population under the FDA's Emergency Use Authorization."*** (CDC)[6]

However, because there are no studies of pregnant women yet, there are no clear recommendations for pregnant women. This is standard for a new drug and is not due to any particular concern with this vaccine.

The **Society for Maternal-Fetal Medicine** ***strongly recommends*** that pregnant individuals have access to COVID vaccines. They recommend that each person have a discussion with their healthcare professional about their own personal choice.[7]

The **American College of Obstetricians and Gynecologists** recommends that the COVID vaccine should ***not*** be withheld from pregnant individuals who meet criteria for vaccination.[8]

What else should I think about to help me decide?

1 Make sure you understand as much as you can about COVID and about the vaccine. Ask a trusted source, like your midwife or doctor. Page 5 has more information about the vaccine.

2 Think about your own personal risk.

Look at the columns below and think about *your* risk of getting COVID (Left). Think about your safety - are you able to stay safe (Right)?

The risks of getting sick from COVID are higher if…	If you are not at higher risk for COVID and…
☐ You have contact with people outside your household who do not wear masks	☐ …you are always able to wear a mask
☐ You are 35 years old or older	☐ …you and the people you live with can socially distance from others for your whole pregnancy
☐ You are overweight	☐ …your community does NOT have high or increasing COVID cases
☐ You have other medical problems such as diabetes, high blood pressure, or heart disease	☐ …you think the vaccine itself will make you very nervous (you are more worried about the unknown risks than about getting COVID)
☐ You are a smoker	☐ …you have had a severe allergic reaction to a vaccine
☐ You are a racial or ethnic minority, or your community has a high rate of COVID infections	
☐ You are healthcare worker[9]	
If you are at a higher risk of getting COVID, it probably makes sense to get the vaccine.	**… it might make sense for you to wait for more information.**

Baystate Health | University of Massachusetts Medical School UMASS

Updated December 14, 2020

What about breastfeeding?

The **Society for Maternal-Fetal Medicine** reports that there is no reason to believe that the vaccine affects the safety of breastmilk.[7] When we have an infection or get a vaccine, our bodies make antibodies to fight the infection. Antibodies formed from vaccines given during pregnancy do pass into the breastmilk and then to the baby to help prevent infections. Since the vaccine does not contain the virus, there is no risk of breastmilk containing the virus.

Summary

1. COVID seems to cause more harm in pregnant women than in women of the same age who are not pregnant.
2. The risks of getting the COVID vaccine during pregnancy are thought to be small but are not totally known.
3. You should consider your own personal risk of getting COVID. If your personal risk is high, or there are many cases of COVID in your community, it probably makes sense for you to get the vaccine while pregnant.
4. Whether to get the vaccine during pregnancy is your choice.

What do pregnant doctors think?

We know COVID can be terrible in pregnancy, and we know the vaccine doesn't contain live virus. As someone who is approaching my third trimester and working on the front lines of this disease, for me the choice is clear, I intend to be first in line as soon as they will let me have one. (Pregnant Emergency Department Doctor)

I am a little nervous about getting something that hasn't been tested in pregnant patients. Early pregnancy is a nerve-wracking time, even without the unknown of a new vaccine. So, I went over the risks and benefits of getting or not getting it as a front-line worker - with myself, my partner, and my doctors. We ended up deciding I should get the vaccine. (Pregnant Emergency Department Doctor)

I am still breastfeeding my baby, and I think the risk of exposing my infant and other children and partner to COVID is far greater than any theoretical risk this novel vaccine may have. I've decided to get vaccinated whenever it becomes available. (Breastfeeding OB/GYN Doctor)

Do you have more questions? Call your doctor or midwife to talk about your own personal decision.

Thoughts about this tool?

Was this decision aid helpful? Please take a moment to give us feedback about this decision aid at https://is.gd/COVIDVac or by scanning the QR code below. We need your help!

Feedback about your experience with the vaccine

If you decide to get the vaccine, you will get a "V-safe information sheet" with instructions about the V-safe website and app for reporting symptoms after your vaccine. This will help researchers track side effects and learn more about how well the vaccine works.

More information about the COVID Vaccine

How does the COVID vaccine work?

- The Pfizer COVID vaccine is an mRNA vaccine (messenger RNA).
- mRNA is not new - our bodies are full of it. mRNA vaccines been studied for the past two decades.
- mRNA vaccines mimic how viruses work. The mRNA is like a recipe card that goes into your body and makes one recipe for a brief time. The recipe is for a small part of the virus (the spike protein).
- When this spike protein is released from cells, the body recognizes it as foreign and the immune system responds. This immune response causes the side effect symptoms (like aches and fever) but leads to improved immunity.
- mRNA breaks down quickly, so it only lasts a brief time.
- This is also how the other viruses like a cold virus work – viruses use our body and cells to make their proteins. Then our immune system attacks those proteins to keep us healthy.
- There is no live virus in this vaccine and there is no way for the vaccine to give people COVID.[5]

What did the research show?

We know that the Pfizer vaccine trial of over 40,000 people has shown that the vaccine lowers a person's chance of getting COVID and severe COVID. In this study, 20,000 people got the vaccine and 20,000 people got a placebo (like a sugar pill).

- After one dose, the vaccine appears to be 50% effective. After 2 doses, the vaccine is 95% effective.
- In other words, **for every 100 people who got COVID in the placebo group, only 5 people got COVID in the vaccine group.**
- There were 9 cases of severe COVID in the placebo group and 1 case in the vaccine group.
- There were no serious safety concerns.

Intended Use: This decision aid is intended for use by pregnant women (and women planning on becoming pregnant) who are considering getting the COVID-19 vaccine, as well as their healthcare providers, and their friends and family. It was created by the *Shared Decision-Making: COVID Vaccination in Pregnancy* working group at the University of Massachusetts Medical School – Baystate. This group consists of experts in the fields of OB/GYN, Maternal-Fetal Medicine, Shared Decision-Making and risk communication, Emergency Medicine, and current COVID-19 research. Questions should be directed to Dr. Elizabeth Schoenfeld, Elizabeth.Schoenfeld@bhs.org. Feedback regarding the utility of this decision aid can be directed through the survey (see link on page 5).

Baystate Health | University of Massachusetts Medical School

Updated December 14, 2020

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Updated December 14, 2020


GUESS WHO'S COMING TO THANKSGIVING DINNER
WHAMMND
Apologies to Norman Rockwell
1616 × 1212

Thank you!